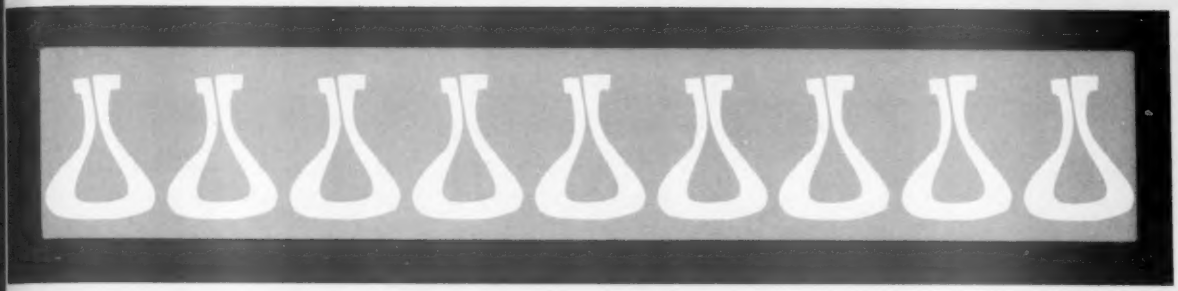

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PSYCHOPHARMACOLOGY ABSTRACTS

NATIONAL INSTITUTE OF MENTAL HEALTH

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

069804 Khanna, K. L.; Takido, M.; Rosenberg, H.; Paul, A. G. College of Pharmacy, University of Michigan, Ann Arbor, Michigan 48104 Biosynthesis of phenolic tetrahydroisoquinoline alkaloids of peyote. *Phytochemistry (Oxford).* 9:1811-1815, 1970.

Data are presented supporting a proposed pathway of biosynthesis of the phenolic tetrahydroisoquinoline alkaloids of peyote from dopamine. It is suggested that meta-0-methylation of dopamine, hydroxylation in the 5 position, para-0-methylation and finally cyclizations yield anhalamine, anhalidine, anhalonidine, apellotine. 21 references. (Author abstract)

070521 Kuriyama, Kinya. Department of Psychiatry, State University of New York, Downstate Medical Center, Brooklyn, New York Association of bromide with the synaptosomal fraction of mouse brain. *Life Sciences (London).* 9(23):1371-1380, 1970.

Binding of bromide by the synaptosomes and mitochondria of mouse brain was studied under a variety of experimental conditions. The synaptosomal uptake of bromide was energy independent and was facilitated by the addition of cations, while the presence of other anions such as nitrate, iodide, pyruvate and lactate inhibited the association of bromide with synaptosomes. Acidification of the incubation medium resulted in the increase of bromide binding with synaptosomes. Brain mitochondria also bound bromide but much less extensively than synaptosomes. The results are consistent with the interpretation that the binding of bromide appears to resemble an anion exchange process. One of the attributes of the bromide binding site on the synaptosomes is the presence of exposed, highly ionized cationic constituents. Furthermore, the results suggest that negative surface charge of the synaptosomes may also be a regulatory factor for the binding. 21 references. (Author abstract modified)

070751 Neal, J. M.; McLaughlin, J. L. Drug Plant Laboratory, College of Pharmacy, University of Washington, Seattle, Washington 98105 Cactus alkaloids: IX. Isolation of N-methyl-3,4-dimethoxy-beta-phenethylamine and N-methyl-4-methoxy-beta-phenethylamine from Ariocarpus retusus. *Lloydia.* 33(3):395-396, 1970.

The isolation of 2 alkaloids from the cactus, Ariocarpus retusus, is described. The natural occurrence of the compounds, N-methyl-3,4-dimethoxy- beta-phenethylamine and N-methyl-4-methoxy-beta-phenethylamine, has been only recently reported and both have been encountered only in other cactus species. Isolation of the crude alkaloids and resolution of the alkaloids by thin layer chromatography are described. The thin layer chromatograms, melting points and infrared spectra of the hydrochlorides of the isolated, crystalline compounds were identical to those of the synthesized hydrochloride derivatives. 15 references.

070779 den Besten, W.; Mulder, D.; Funcke, A. B. H.; Nauta, W. Th. N.V. Kon. Pharm. Fabr. v/h Brocades-Stheeman en Pharmacia, Looiersgracht 27-39, Amsterdam, The Netherlands The effect of alkyl substitution in drugs. *Arzneimittel-Forschung (Aulendorf).* 20(4):538-542, 1970.

The synthesis of potential orphenadrine metabolites is described. Eight of these, one of them called tofenacin, were screened in vitro and in vivo in animals, guinea pigs, and mice. Although it is unlikely that these metabolites are exhaustively responsible for the pharmacological effects of orphenadrine, it is likely tofenacine with its marked anticataleptic activity as well as the other metabolites contribute to this effect. An analogy seems to exist between the activity of orphenadrine and tofenacine, like that between imipramine and desimipramine. 19 references. (author abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

070218 Sourkes, T. L. Laboratory of Chemical Neurobiology, Department of Psychiatry, McGill University, Montreal, Quebec, Canada Twenty-five years of biochemical psychiatry. *Canadian Psychiatric Association Journal (Ottawa).* 15(6):625-629, 1970.

Recent biochemical research in psychiatry is reviewed, and the contribution of chemical neurobiology to an expanded knowledge of the chemistry of the brain is examined. The areas of

particular significance to psychiatry are identified as: 2) research involving the mechanism of action of tranquilizers, antidepressant drugs, sedatives and convulsants, as well as many agents whose predominant action is upon the autonomic nervous system and (2) studies on the metabolic function of brain biogenic amines. Recent discoveries regarding the neurobiology of brain biogenic amines have led to new concepts of psychotic states and initiated attempts to link specific brain damage with characteristic changes in the function of the central nervous system and behavioral patterns. In addition, earlier hypothesis has been confirmed that a causal relationship exists between brain dopamine concentrations and biochemical abnormality, as illustrated in research in Parkinson's disease. Further studies have also established the role of L-dopa and other brain biogenic amines in dysfunctions of the extrapyramidal system. It is anticipated that such biochemical research will lead to further studies involving the perceptive, cognitive, and affective functions of the brain, as well as development of more effective drugs for treatment of the major mental disorders. 11 references.

070839 Davenport, John W. Regional Primate Research Center, University of Wisconsin, Madison, Wisconsin Cretinism in rats: enduring behavioral deficit induced by tricyanoaminopropene. ***Science.*** **167(3920):1007-1009, 1970.**

Rats reared on diets containing tricyanoaminopropene, the antithyroid compound that stimulates RNA synthesis, showed a deficit in performance on automated closed field maze tests many weeks after discontinuation of the drug. The rats were also tested while still receiving the drug, and performance deficits were indicated in tests of Y-maze reversal and manual closed field maze performance; rats treated with the drug and with thiouracil behaved in a highly similar fashion on several tasks. No evidence of facilitation by tricyanoaminopropene appeared in any of the eight learning situations used. Exposure to tricyanoaminopropene before and after birth, at doses sufficient to produce anatomical cretinism, apparently induces an enduring behavioral deficit which is similar to that of neonatal thyroidectomy induced cretinism in rats and which parallels the mental retardation associated with human cretinism. 20 references. (author abstract)

070926 Metys, J; Metysova, J. Research Institute for Pharmacy and Biochemistry, Kourimska 17, Prague 3, Czechoslovakia Comparative pharmacological study of neuroleptics in rodents. ***Activitas Nervosa Superior (Praha).*** **12(1):43-44, 1970.**

In experiments on mice and rats, the neuroleptics octoclothepin and methiothepin were compared with clinically used substances of this type. Several behavioral parameters were tested. No considerable differences between medium effective doses were found in spontaneous locomotor activity, motility in an observational procedure, gnawing activity, responsiveness to nociceptive stimulation, and motor coordination. Both tested drugs showed a high neuroleptic activity; octoclothepin exhibited many of the same properties as perphenazine. 7 references.

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

069595 Shen, Fu-Hsiug; Loh, Horace H.; Way, E. Leong. Stamford Hospital, 190 West Broad Street, Stamford, Connecticut 06902 Brain serotonin turnover in morphine tolerant and dependent mice. ***Journal of Pharmacology and Experimental Therapeutics.*** **175(2):427-434, 1970.**

The rate of serotonin (5-HT) synthesis in the brains of mice rendered tolerant to and physically dependent on morphine either by s.c. implantation of a morphine pellet for 3 to 4 days or by daily s.c. injections of increasing doses of morphine was found to be about twice that of control animals receiving a placebo implant or daily saline injections. Inhibition of brain 5-HT synthesis by p-chlorophenylalanine was accompanied by a decrease in tolerance and dependence development to morphine. The concomitant administration of naloxone to reduce tolerance and physical dependence development to daily injections of morphine resulted also in a decrease in the rate of brain 5-HT synthesis. Although the roles of other biogenic amines have not been excluded, the results suggest that increased brain 5-HT synthesis may be associated with tolerance and physical dependence development to morphine in the mouse but do not establish a causal relationship. 24 references. (Journal abstract)

069596 Sanders-Bush, E.; Sulser, F. Department of Pharmacology, Vanderbilt University, School of Medicine, Nashville, Tennessee 37203 p-Chloroamphetamine: in vivo investigations on the

mechanism of action of the selective depletion of cerebral serotonin. *Journal of Pharmacology and Experimental Therapeutics.* 175(2):419-426, 1970.

The present investigations were undertaken to study the mechanism by which p-chloramphetamine decreases both serotonin (5-HT) and 5-hydroxyindole acetic acid in the brains of rats. 1) Doses of p-chloroamphetamine, which markedly reduced the level of endogenous 5-HT in brain, failed to decrease labeled 5-HT derived from either intraventricularly administered 5-HT-H3 or 5-hydroxytryptophan-Cl4. Under similar conditions, reserpine and RO 4-1284 caused a striking reduction of both the endogenous and the labeled 5-HT. 2) p-Chloroamphetamine partially blocked the increase of endogenous brain 5-HT but not that of brain norepinephrine, after monoamine oxidase inhibition by pargyline. 3) The increase in brain 5-hydroxyindole acetic acid resulting from the administration of probenecid was almost completely blocked in animals treated 48 and 24 hours previously with p-chloroamphetamine. This blockade was not evident when p-chloroamphetamine was administered 10 minutes prior to probenecid. 4) Like p-chlorophenylalanine, p-chloroamphetamine caused a decrease in the amount of 5-HT-Cl4 in brain (formed from intraventricularly administered tryptophan-Cl4; however, it did not change the amount of 5-HT-Cl4 derived from intraventricular 5-hydroxtryptophan-Cl4. 5) p-Chloroamphetamine did not alter the level of either endogenous tryptophan or tryptophan-Cl4 taken up into the brain from the ventricular system. On the basis of these experimental data, it is concluded that p-chloroamphetamine impairs the synthesis of cerebral 5-HT. Moreover, the results of thesestudies in vivo implicate an inhibition of cerebral tryptophan hydroxylase in the simultaneous lowering of cerebral 5-HT and 5-hydroxyindole acetic acid by p-chloroamphetamine. 25 references. (Journal abstract)

069645 Shemberg, K.; Green, P. C.; Gliner, J. Bowling Green State University, Bowling Green, Ohio 43402 A note on the effects of chlorpormazine upon ulceration in the rat. *Psychonomic Science.* 20(5):272-273, 1970.

Research was conducted to study the effects of chlorpormazine in an ulcerogenic stress situation and to test varying concentrations of this drug in order to detect possible protective effects. Four groups of rats were exposed to a highly ulcerogenic procedure. Three experimental groups were given programmed injections of 3 different concentrations of chlorpormazine and a control group received physiological saline. All drug concentrations significantly reduced ulceration relative to controls. The lowest concentration proved least effective in this regard, but no simple linear relationship was found between drug concentration and frequency of ulceration. A tentative hypothesis regarding an all or noneprotective function of the drug was suggested, and parameters for future research outlined. 6 references. (Author abstract modified)

070334 Ito, Koichi; Miyagishi, Tsutomu; Takahata, Naohiko. Department of Psychiatry and Neurology, Hokkaido University School of Medicine, Hokkaido, Japan An electron microscopic study of axonal changes in the cerebellum of diphenyl-hydantoin intoxicated rats: the formation of the so-called 'honeycomb structure' in the axoplasm. *Folia Psychiatrica et Neurologica Japonica (Niigata).* 24(1):49-58, 1970.

The ultrastructural axonal changes found in the cerebellar parenchyma of diphenyl-hydantoin (DPH) intoxicated rats were studied. Various types of unusual structures including vacuoles, tubules and honeycomb structures were observed in the axons of the granular cell layer. Through the observations of these structures, it was concluded that there are 2 types of honeycomb structures and that a developmental sequence of stages from vacuoles to honeycomb structures exists, which can be summarized as follows: vacuoles with fine granules on their membranes appear showing some relations with the mitochondria; from the vacuoles 1 or more tubules with fine granules spirally arrayed thereon sprout and gradually lengthen; the lengthened tubules are assembled and arrayed in parallel and the cut ends of tubules show honeycomb structures; each of the lengthened tubules swells torturously and as a result another type of honeycomb structure is seen. It is suggested that these singular structures may well have resulted from metabolic disorders arising from DPH intoxication. Photographic plates of the axonal changes are appended. 23 references. (Author abstract modified)

070443 Sofia, R. Duane; Barry, Herbert, III. Dept. of Pharmacology, Univ. of Pittsburgh, Pittsburgh, Pennsylvania Depressant effect of delta 1-tetrahydrocannabinol enhanced by inhibition of its

metabolism. *European Journal of Pharmacology (Leiden).* 13:134p137, 1970.

Prolongation of barbital sleeping time in mice by delta 1-tetrahydrocannabinol (delta 1-THC), 10 and 20 mg/kg, i.p.,was enhanced when its hydroxylation to the 7-hydroxy metabolite was blocked by SKF 525-A (beta-diethylaminoethyldiphenylpropylacetate hydrochloride), 12.5and 25 mg/kg, i.p.,which inhibits the drug metabolizing microsomal enzymes. The SKF-525 alone had slight effect. Sleeping time was reliably longer after the lower dose of both compounds than after the higher dose of either one alone. This central depressant effect of delta 1-THC is thus due to the parent compound rather than its metabolite. 13 references. (Author abstract)

070542 Tonge, Sally R.; Leonard B. E. Department of Pharmacy, Liverpool Polytechnic (Science and Engineering), Byrom Street, Liverpool, England The effect of some hallucinogenic drugs on the amino acid precursors of brain monoamines. *Life Sciences (Oxford).* 9(23):1327-1335, 1970.

The effect of some hallucinogenic drugs on the amino acid precursors of brain monoamines is studied in rats. Four structurally dissimilar hallucinogenic drugs, phencyclidine, Ditran, lysergic acid diethylamide (LSD) and mescaline, were administered intraperitoneally to rats of the Wistar strain. The gross behavioral pattern was used as an approximate guide to the course of action of the drugs, in absence of a satisfactory specific test for hallucinogenic activity. Blood samples and whole brains were taken from animals at 7 intervals after drug administration: 0, 10, 20, 40, 60, 100 and 180 min. The behavioral changes are described elsewhere. Changes in brain and plasma concentrations of tryptophan and tyrposine are reported. Phencyclidine, Ditran and mescaline all caused depletion of endogenous tryptophan from brain tissue and from plasma in rats. LSD was found to produce an elevation of brain tryptophan levels, but a depletion of plasma tryptophan. All 4 hallucinogens produced elevations of brain tyrosine concentrations accompanied by decreased plasma levels of the amino acid. The results of the study are discussed. 17 references.

070823 Mueller, F. O.; Magos, L. Toxicology Research Unit, Medical Research Council Laboratories, Carshalton, Surrey, England Reversible lenticular opacities induced in rats by emotional stress. *Experientia (Basel).* 26(2):169-170, 1970.

The effects of different catacholamines on the lens were studied in Porton-Wistar rats pretreated with 150mg/kg s.c. of pargyline hydrochloride. There was a significantly high incidence of dense lenticular opacities in rats pretreated with pargyline hydrochloride, and then exposed to a stressful situation. The cataracts produced are reversible, and are a result of the release of noradrenalin and other catecholamines induced by emotional stress. The iridial noradrenalin released in the eye by emotional stress is believed to change the outflow and the composition of the aqueous humor. 11 references.

070825 Vernadakis, Antonia. Departments of Psychiatry and Pharmacology, University of Colorado Medical Center, Denver, Colorado 80220 Effects of chlorpromazine on neural tissue in culture. *Experientia (Basel).* 26(2):171-172, 1970.

The effects of chlorpromazine were studied on the acetylcholine esterase activity and protein content of cerebellar and spinal cord explants removed from chick embryos at 9, 16, and 20 days of incubation and maintained in culture. Spinal cord explants, but not cerebellar explants, were sensitive to chlorpromazine in culture, and acetylcholine esterase activity was significantly higher in spinal cord explants removed from the 9 day old chick embryo. These results may reflect an enzyme induction activity by chlorpromazine. 13 references.

070951 Ladisich, W.; Volbehr, H.; Matussek, N. Max Planck Institut fur Psychiatrie, Kraepelinstrasse, Munich, Germany Biochemical and behavioral effect of amphetamine in DMI + RO 4-1284 induced hyperactivity. *Activitas Nervosa Superior (Praha).* 12(1):83-84, 1970.

The paradoxical effect of amphetamine on the motor hyperactivity of rats induced by desmethylimipramine and the benzoquinolizine, RO 4-1284 is reported. Amphetamine reduced the hyperactivity of rats pretreated with desmethylimipramine (DMI). Tritiated norepinephrine was used to study the metabolism of catecholamines in these experiments. After intracisternal injection, there was an increase in normetanephrine in the rats premedicated with DMI and amphetamine. This increase is at least partly responsible for amphetamine sedation.

070953 Benes, V.; Benesova, O. Institute of Industrial Hygiene and Occupational Diseases,

Prague,Czechoslovakia Monoamines and the reactivity of rats with different types of higher nervous activity. ***Activitas Nervosa Superior (Praha).*** **12(1):88-90, 1970.**

The biochemical correlates of higher nervous activity and the intensity of exploratory activity were studied in 60 rats. The relationship of brain monoamine levels reactivity to stress were evaluated. No differences were found in the levels of dopamine. A statistically significant increase in elimination of noradrenaline was reported. Emotional and anxious reactions can thus be accompanied by an increase in noradrenaline excretion. 11 references.

071703 Lindemann, M.; Schilter, R.; Sinkwitz, K.-D. Dept. of Physiology, Medical Faculty, Humboldt University, Berlin, West Germany The influence of the ganglionic blocking agent ganlion on viscerovisceral and viscerocerebral reactions of the cat. ***Conditional Reflex.*** **5(2):97-108, 1970.**

In 21 subacute or chronic cats the influence of gallbladder distention on heart rate, respiratory movements, bioelectrical activity of the cerebral cortex and motor behavior were studied under normal conditions and after intraperitoneal administration of a ganglionic blocking agent. In control groups without administration of the drug, changes of heart and respiratory rates were observed during the mechanical stimulation of the gallbladder. These effects were independent of a sleeping or non-sleeping state of the animal. In some cases viscerovisceral reactions could be accompanied by an arousal reaction. After administration of the blocking agent in amounts ranging between 5 to 50 mg/kg body weight the viscerovisceral reactions were inhibited, whereas the behavioral arousal remained. 32 references. (journal abstract)

071783 Mitoma, Chozo. Life Sciences Division, Stanford Research Institute, Menlo Park, California 94025 Metabolic studies on trimethoxyamphetamines. ***Proceedings of the Society for Experimental Biology and Medicine.*** **134(4):1162-1164, 1970.**

The metabolism of dl-2,4,5-trimethoxyamphetamine (TMA-2) and dl-2,3,4-trimethoxyamphetamine (TMA-3) in rats was investigated to determine its relationship (if any) to the observed relative potency of these compounds as psychotomimetic agents. Although TMA-2 is a more potent psychotomimetic agent than TMA-3, the concentration of TMA-3 in the brain at 30 minutes after injection was 17.0micrograms, and the concentration of TMA-2 was 5.3micrograms. Since the peak effect of these compounds in behavioral studies was observed to be 30 min after injection, apparently, the amount that enters the brain is not the factor that determines the psychotomimetic properties of these compounds. In vitro studies with rat and rabbit liver homogenates indicated that TMA compounds were metabolized primarily by O-demethylation, similarly to mescaline, but were not measurably deaminated as is the case with amphetamine. The TMA-demethylating enzyme is associated with liver microsomes and its activity is not elevated by pretreatment with phenobarbital. 8 references.

071790 Evans, Hugh L.; Patton, R. A. Department of Radiation Biology and Biophysics, School of Medicine and Dentistry, University of Rochester, Rochester, New York 14620 Scopolamine effects on conditioned suppression: influence of diurnal cycle and transitions between normal and drugged states. ***Psychopharmacologia (Berlin).*** **17(1):1-13, 1970.**

Two hundred twenty four naive rats, were exposed to either a drug induced state (1mg/kg scopolamine) or an undrugged state (saline control) at each stage of a 3 stage procedure (they were trained to lick a tube, stage one, then exposed to classical fear conditioning in the absence of the tube, and finally tested for conditioned suppression of licking). Animals tested in the midst of the dark period of the daily light dark cycle displayed a failure of conditioned suppression if conditioning had occurred under the novel state; suppression was less consistently impaired in animals tested at the midst of the photoperiod. All animals exposed to a consistent drugged or undrugged state displayed conditioned suppression. Apparently, experimental procedures frequently employed in studying drug manipulations of learning and memory may be biased against the transfer of training to the test situation. Scopolamine effects, often attributed to changes in learning or memory, may often represent a weakening in stimulus control of behavior resulting from transitions between drugged and undrugged states. Several factors, variation in sensitivity, states of water deprivation, specific neurochemical phenomena, are suggested as contributing to the diurnal difference in drug effects. 43 references. (author abstract modified)

071791 Lingjaerde, O., Jr. Universittets Psykiatriske Klinikk, Vinderen, Oslo 3, Norway Inhibitory effect of two newer antidepressants, Lu 5-003 and Lu 3-010, on serotonin uptake in human blood platelets in vitro. ***Psychopharmacologia (Berlin).*** **17(1):94-99, 1970.**

Two new drugs currently under investigation for antidepressant properties are 1-(3-methylaminopropyl)-1-phenyl-3,3-dimethyl - thiophthalane hydrochloride (Lu 5-003) and the corresponding phthalane derivative (Lu 3-010). Their inhibitory effect on 5-hydroxytryptamine uptake in human blood platelets in vitro has been studied in comparison with some well known tricyclic antidepressants. These newer drugs were found to be about 10 times less potent in this respect than imipramine and amitriptyline, and several times less potent than desipramine and nortriptyline. The inhibitory effect of Lu 5-003, which seems to be the more clinically promising, was found to be of the competitive type. The possible correlation between inhibitory effects on the serotonin pump and the antidepressant effect is of theoretical interest and practical importance, as such correlation would support the serotonin hypothesis of manic-depressive illness. The finding that these 2 two new drugs possess strong antidepressant properties would contraindicate a simple serotonin hypothesis. 20 references. (author abstract modified)

071942 DiCarlo, Frederick J.; Viau, Jean-Paul. Department of Biochemistry, Warner-Lambert Research Institute, Morris Plains, New Jersey 07950 Prazepam metabolites in dog urine. ***Journal of Pharmaceutical Sciences.*** **59(3):322-325, 1970.**

Within 24 hr after receiving a single oral dose (10mg/kg) of 14C labeled prazepam, 2 dogs excreted small quantities (4.6% and 1.8%) of the radioactivity in the urine. Most of the drug was transformed apparently by oxidative enzymes of the liver microsomes. The major drug metabolite was oxazepam glucuronide. Thin layer chromatography showed the presence of at least 8 radioactive compounds in the urine. Six of these accounted for 86% of the 14C in the urine from Dog 1 and 95% from Dog 2. These compounds and their contributions to the urinary radioactivity were, for Dogs 1 and 2, respectively: prazepam, 1% and 0.2%; desalkylprazepam, 2% and 0.4%; 3-hydroxyprazepam glucuronide, 9% and 11%; oxazepam, 14% and 3%; oxazepam glucuronide, 52% and 72%; and 4'-hydroxyoxazepam glucuronide, 8% for each. Prazepam is considered to serve as the precursor to a series of metabolites with tranquilizer activity. 19 references. (author abstract modified)

072030 Grunden, Lee R.; Marley, E. Division of Pharmacology, College of Pharmacy, University of Arizona, Tucson, Arizona 85721 Effects of sympathomimetic amines injected into the third cerebral ventrical in adult chickens. ***Neuropharmacology (Oxford).*** **9(2):119-128, 1970.**

The effects of sympathomimetic amines injected into the third cerebral ventricle of unanesthetized adult fowls were studied. Catecholamines (0.5micromole) produced behavioral and electrocortical sleep accompanied by hypothermia and a small decrease in electromyographic activity, although dopamine had minimal effects. The soporific and hypothermic effects observed were qualitatively similar to those resulting from small intravenous doses of catecholamines in young chickens. Equimolar doses of beta-phenethylamine and dexamphetamine were ineffective, while 0.5micromole of 5-hydroxytryptamine elicited biphasic behavioral and electrocortical effects. Saline (20 microliters) did not alter behavior, electrocortical or electromyographic activity, but moderate elevation of core temperature was sometimes observed. These results provide additional evidence for a differential central action of sympathomimetic amines depending on their chemical structure and route of administration. 38 references. (author abstract modified)

072031 Chase, T. N.; Katz, R. I.; Kopin, I. J. Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland 20014 Effect of diazepam on fate of intracisternally injected serotonin-C14. ***Neuropharmacology (Oxford).*** **9(2):103-108, 1970.**

The influence of diazepam on the disposition of intracisternally injected serotonin-C14 was studied in the rat. Pretreatment with diazepam failed to affect the uptake of serotonin by brain. Whole brain levels of serotonin-C14 and 5-hydroxyindoleacetic acid-C14, substantially above control levels, were found in diazepam treated rats killed 3 hours after serotonin-C14 administration. The drug markedly retarded the efflux of intracisternally administered 5-hydroxyindoleacetic acid-C14 but had no effect on metaraminol-H3, a monoamine which is not metabolized in brain. These findings suggest that diazepam may act on

mechanisms subserving the transport of 5-hydroxyindoleacetic acid from brain as well as on the cerebral metabolism of serotonin. 35 references. (author abstract modified)

072034 Elliott, R. C. Department of Biology, Brunel University, Woodlands Avenue, London W3, England The action of central depressant drugs on the spontaneous discharge of action potentials in the superior cervical sympathetic trunk of the cat. ***Neuropharmacology (Oxford).*** **9(2):129-136, 1970.**

Spontaneous action potentials were recorded in strands dissected from the preganglionic superior cervical trunk of anesthetized cats. The rate of discharge of spontaneous action potentials was reduced by 63.7% after i.v. administration of 0.5mg/kg of chlorpromazine. Local anesthetic action was insufficient to account for the rate reduction; it is probably attributable to a centrally mediated action. Intravenous administration of 1 mg/kg of perphenazine reduced the rate of dischargeby 61.6%, and an i.v. dose of 10 mg/kg of pentobarbitone reduced the rate of discharge by 66.4% (an i.v. dose of 2 mg/kg of pentobarbitone had little or no effect). Results with hydroxyzine and benactyzine were variable. Hydroxyzine had no effect in some experiments, but in others 2 mg/kg i.v. produced a reduction of 25 to 70%. Benactyzine had little effect, the greatest reduction was only 28%. It is concluded that some tranquilizers reduce the rate of discharge in a preganglionic sympathetic nerve, and that this may be a contributory factor in producing their psychotropic effects in man. 16 references. (author abstract modified)

072067 Heinemann, H.; Hartmann, A.; Stock, G.; Sturm, V. Physiologisches Institut der Universitat Heidelberg, Akademiestrasse 3, 69 Heidelberg, Germany /The effect of Medazepam on the thresholds of subcortical limbic stimulus responses, measured in unanesthetized, unrestrained cats./ Die Wirkung von Medazepam auf Schwellen subcorticaler, limbischer Reizantworten, gemessen an unnarkotisierten, frei beweglichen Katzen. ***Arzneimittel-Forschung (Aulendorf).*** **20(3):413-415, 1970.**

The effect and sites of action of Medazepam (a new benzodiazepine derivative) was investigated by measuring response potentials evoked in 5 unanesthetized, unrestrained cats. The agent was administered intravenously as a continuous injection to electrical stimulation of the amygdaloid nucleus, septum, dorsomedial nucleus and hippocampus during continuous i.v. injection. Threshold potentials in the amygdaloid nucleus were lowered with the exception of the hippocampus. The thresholds of the joints between 2 nuclear areas may be influenced by Medazepam in both directions of the induced response. The elevation of all the response thresholds of the joints of the ventral hippocampus may be responsible for the sleep inducing and anticonvulsive effects of the drug. 23 references. (author abstract modified)

072119 Carl, Juanita L.; King, Lucy J. Department of Psychiatry, Washington University School of Medicine, St. Louis, Missouri Hexose and pentose phosphates in brain during convulsions. ***Journal of Neurochemistry (London).*** **17(2):293-295, 1970.**

Assays for hexose and pentose phosphates were carried out in brains of convulsing mice with or without the administration of phenobarbitol prior to electrical stimulation to determine whether or not levels of these substrates are altered under these conditions. Xylulose-5-P in brains of animals which received no phenobarbitone decreased within 10 seconds after convulsive stimulation. Glucose-6-P and fructose-6-P decreased rapidly within 10 seconds but then rose again to preconvulsion levels by 50 seconds. Administration of phenobarbital to mice prior to convulsive electrical stimulation greatly diminished the changes in hexose and pentose phosphates. Data suggest that during the greatly increased metabolic rates accompanying convulsions, intermediates of the pentose phosphate pathways are depleted just like substances of the glycolytic pathway. 6 references.

072120 Uretsky, N. J.; Iversen, L. L. Department of Pharmacology, University of Cambridge, Cambridge,England Effects of 6-hydroxydopamine on catecholamine containing neurones in the rat brain. ***Journal of Neurochemistry (London).*** **17(2):269-278, 1970.**

After the intraventricular injection of 6-hydroxydopamine (6-OHDA), there was a long lasting reduction in the brain concentrations of noradrenaline (NA) and dopamine (DA). A high dose of 6-OHDA which depleted the brain of noradrenaline and dopamine had no significant effect on brain concentrations of 5-hydroxytryptamine (5-HT) or gamma aminobutyric acid (GABA). The fall in catecholamines was accom-

panied by a long lasting reduction of the activities of tyrosine hydroxylase and DOPA decarboxylase in the hypothalamus and striatum, areas in the brain which are rich in catecholamine containing nerve endings. There was, however, no consistent effect on catechol-O-methyl transferase or monoamine oxidase activity in these brain regions. The initial accumulation of (3H)NA into slices of the hypothalamus and striatum was markedly reduced 22 to 30 days after 6-OHDA treatment. These results are consistent with the evidence in the peripheral sympathetic nervous system that 6-OHDA causes a selective destruction of adrenergic nerve endings and suggest that this compound may have a similar destructive effect on catecholamine neurons in the central nervous system. 38 references. (author abstract modified)

04 MECHANISM OF ACTION: BEHAVIORAL

069530 Lawrence, Carl W.; Haynes, Jack R. Travis State School, Denton, Texas Epinephrine and nor-epinephrine effects on social dominance behavior. *Psychological Reports.* 27(1):195-198, 1970.

The behavioral effects of intraperitoneal injections of epinephrine and norepinephrine on established dominant submissive relationships were compared. Since approach avoidance behavior has been found affected by those two hormones, it was assumed that injections of epinephrine and norepinephrine would also have differential effects on social dominance behavior. It was hypothesized that l) Ss receiving an injection of epinephrine would show a significantly greater submissive response than when under a condition of noninjection or norepinephrine. 2) Ss receiving an injection of norepinephrine would show a significantly greater dominant response than when under the condition of noninjection or epinephrine. The results showed that all conditions were significantly different from each other, with the greatest amount of dominance behavior being shown under norepinephrine and the greatest submissive behavior under epinephrine. These results indicate that a dominant submissive relationship can be altered by these 2 drugs. It was concluded that epinephrine and norepinehprine may have differential effects on social dominance behavior. 5 references. (Author abstract modified)

069593 McMillan, D. E.; Wolf, P. S.; Carchman, R. A. Department of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, North Carolina 27514 Antagonism of the behavioral effects of morphine and methadone by narcotic antagonists in the pigeon. *Journal of Pharmacology and Experimental Therapeutics.* 175(2):443-458, 1970.

The effects of narcotics and narcotic antagonists, alone and in combination, were studied on the schedule controlled behavior of the pigeon. Morphine and methadone increased the rate of responding under the fixed interval component of a multiple fixed interval, fixed ratio schedule at low dose levels in some birds, and at higher dose levels they decreased the rates of responding under both components in all birds. The effects of narcotic antagonists were much like the effects of morphine and methadone. Naloxone, which has been considered to be a relatively pure narcotic antagonist, affected the schedule controlled behavior of the pigeon in the same way as other narcotic antagonists and with a greater potency than some. Narcotic antagonists blocked both the rate increasing and rate decreasing effects of morphine. The order of potency of the narcotic antagonists for blocking the rate decreasing effects of morphine was: naloxone equals cyclazocine greater than nalorphine greater than pentazocine. This antagonism of the rate decreasing effect of morphine seemedto be specific for narcotic analgesics, since naloxone and cyclazocine blocked the effects of methadone as well as morphine, but naloxone did not block the rate decreasing effect of chlorpromazine and cyclazocine. Although d-amphetamine could reverse the rate decreasing effects of morphine, the degree of reversal was proportional to the rate increasing effects of d-amphetamine, which was unlike the antagonism of the rate decreasing effects of morphine by narcotic antagonists. The rate increasing effects of morphine and d-amphetamine were additive, rather than antagonistic. 32 references. (Journal abstract)

069594 Dewey, William L.; Harris, Louis S.; Howes, John F.; Nuite, Jo Ann. Department of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, North Carolina 27514 The effect of various neurohumoral modulators on the activity of morphine and the narcotic antagonists in the tail-flick and phenylquinone tests. *Journal of Pharmacology and Experimental Therapeutics.* 175(2):435-442, 1970.

The effect of a number of agents which alter central neurohumeral tone on the activity of morphine and the narcotic antagonists in the tail flick and the phenylquinone tests have been investigated. In general, an increase in central adrenergic tone caused an increase in the activity of morphine in the tail flick test. However, some exceptions were observed which suggest mechanisms other than changes in neuromodulator tone might be responsible for the alterations of the potency of morphine. A number of these have been investigated and were found not to be contributing factors. Drugs which decrease adrenergic tone decreased the activity of morphine in this procedure. Alterations in adrenergic tone did not affect the analgesic activity of the antagonists. 5-Hydroxtryptophan caused an increase in the potency of morphine in the tail flick procedure, thus indicating a possible involvement of central serotonergic mechanisms. A correlation between adrenergic or cholinergic tone and activity in the p-phenylquinone test was not evident. The significance of these results and the resultant validity of these procedures as screens for analgesics is discussed. 25 references. (Journal abstract)

069610 Witters, Weldon L.; Foley, C. W. Ohio University, Athens, Ohio 45701 Effects of agroclavine on wheel-turning activity in mice. ***Psychonomic Science.*** **21(3):175-176, 1970.**

To explore the relationship between agroclavine dosage level and general activity and compare results with those of Harsh, Witters and Yarem Ko with elymoclavine, 5 groups of mice were administered agroclavine, a drug similar to LSD, and had activity level recorded. Over 5 consecutive days smaller dosage levels either enhanced or produced little change in wheel running activity, while higher dosages produced a decrement. These results are similar to those studies using elymoclavine although larger amounts of agroclavine are needed to produce similar results. 10 references. (Journal abstract modified)

069637 Winson, Jonathan; Miller, Neal E. Rockefeller University, New York, New York 10021 Comparison of drinking elicted by eserine or DFP injected into preoptic area of rat brain. ***Journal of Comparative and Physiological Psychology.*** **73(2):233-237, 1970.**

Injection of eserine into the preoptic area of the rat brain will cause water satiated animals to drink when water is made available 60 min. after injection but not beyond that time, whereas injection of diisopropyl fluorophosphate (DFP) will cause drinking up to 210 min. after injection. The drinking is presumably caused by inhibition of cholinesterase at cholinergic synapses. The cessation of drinking in the case of eserine, a reversible inhibitor, probably results from a drop in concentration at the site with time; in the case of DFP, a reportedly irreversible inhibitor, the cessation may be due to the resynthesis of a known isozyme of cholinesterase with a half life of 3 hr. or to spontaneous reactivation of the enzyme. 11 references. (Author abstract)

069738 Graeff, F. G.; Schoenfeld, R. I. Department of Pharmacology, Faculty of Medicine, Ribeirao Preto, Sao Paulo, Brazil Tryptaminergic mechanisms in punished and nonpunished behavior. ***Journal of Pharmacology and Experimental Therapeutics.*** **173(2):277-283, 1970.**

The dose effect relationships of 2 tryptaminic antagonists, methysergide and bromolysergic acid, and the agonist, alpha-methyltryptamine on key pecking behavior of the pigeon were determined. A multiple fixed interval 5 minute fixed ratio 30 response food presentation schedule and a concurrent fixed interval 5 minute food, fixed ratio 30 electric shock punishment schedule were used. Lower doses of the 2 tryptaminic antagonists increased low response rates occurring at the beginning of the fixed interval component of the multiple schedule and the overall response rates of the punished fixed interval. They also increased the high overall rates of responding during the fixed ratio. Higher doses of methysergide and bromolysergic acid decreased high rates of responding occurring at the end of the fixed interval and the fixed ratio components of the multiple schedule. Alpha-methyltryptamine produced only decreases in responding with both schedules studied. These results suggest the existence of a tryptaminergic mechanism involved in behavioral inhibition. 38 references. (Author abstract)

070083 Iwahara, Shinkuro; Sugimura, Takeshi. Tokyo University of Education, Tokyo, Japan Effects of chlordiazepoxide on black-white discrimination acquisition and reversal in white rats. ***Japanese Journal of Psychology (Tokyo).*** **41(3):142-150, 1970.**

An investigation of the effects of chlordiazepoxide on black - white discrimination acquisition and reversal in white rats is discussed. Two groups of male albino rats were run 20 trials

per day on a black - white discrimination, motivated by electric shock. One group was injected with 2 ml/kg of physiological saline (SAL) and the other with 20 mg/kg of chlordiazepoxide (CDP) (2 ml/kg of a 10 mg/ml solution), both intraperitoneally, 30 min. prior to the first daily trial. Two days after reaching criterion, the rats were given reversal training. Half the animals in each group were changed in drug state and the rest were not changed, and thus 4 groups (SAL-SAL, SAL-CDP:CDP-SAL, CDP-CDP) were run as in acquisition except the stimulus incentives were reversed. Acquisition was slightly but significantly depressed by CDP, while reversal learning was substantially retarded by the drug. Percent errors on the first reversal day clearly indicated a dissociative effect: that is, the rats without drug - state change (SAL-SAL, CDP-CDP) made more errors than those with such change (SAL-CDP, CDP-SAL). In addition, those rats given drug during acquisition were better in performance than those which had been treated with saline. A depressant effect of CDP upon discrimination learning was explained in terms of the drug's inhibitory action on negative incentives. The dissociated performance found on the first reversal day was explained in terms of generalization decrements. 20 references. (Author abstract modified)

070732 Carter, Vernon L., Jr.; Back, Kenneth C.; Farrer, Donald N. Aerospace Medical Research Laboratory, Aerospace Medical Division, Air Force Systems Command, Wright-Patterson Air Force Base, Ohio 45433 The effect of bromotrifluoromethane on operant behavior in monkeys. *Toxicology and Applied Pharmacology.* 17:648-655, 1970.

The effect of bromotrifluoromethane on operant behavior is investigated in monkeys and in higher concentrations resulted in impaired performance. In the study, 7 monkeys trained on continuous and discrete avoidance performance tasks were exposed to concentrations of bromotrifluoromethane (CBrF3) ranging from 10.5% to 42.0%. Significant performance decrements were observed in all subjects during exposures of 20-25% CBrF3. Higher concentrations resulted in impaired performance to the point of complete disruption of operant behavior in some subjects. No visible signs of central nervous system depression or analgesia accompanied this loss of ability to perform on conditioned performance tasks. These results suggest that the mechanism by which CBrF3 causes impaired performance differs from the central nervous system depression and analgesia produced by halogenated anesthetics. 6 references. (Author abstract modified)

070921 Taylor, Kenneth M.; Snyder, Solomon H. Departments of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205 Amphetamine: differentiation by d and l isomers of behavior involving brain norepinephrine or dopamine. *Science.* 168(3938):1487-1489, 1970.

d-Amphetamine is markedly more potent an inhibitor of catecholamine uptake by norepinephrine neurons in the brain than is l-amphetamine, whereas the two isomers are equally active in inhibiting catecholamine uptake by the dopamine neurons of the corpus striatum. In behavioral studies, d-amphetamine is ten times as potent as l-amphetamine in enhancing locomotor activity, while it is only twice as potent in eliciting a compulsive gnawing syndrome. This suggests that the locomotor stimulation induced by amphetamine involves central norepinephrine, while dopamine neurons play an important role in the induced compulsive gnawing behavior. Assessment of differential actions of d-amphetamine and l-amphetamine may be an efficient method to differentiate behaviors involving norepinephrine or dopamine in the brain. (author abstract)

070948 Zabojnikova, M.; Kovalcik, V. Farmakologicky Ustav LF KU, Sasinkova 4, Bratislava, Czechoslovakia Interaction of some psychotropic drugs with analgesics. *Activitas Nervosa Superior (Praha).* 12(1):71-72, 1970.

The antinociceptive activity of desmethylimipramine (DMI) and prothiadene, their influence on the activity of analgesics and their antireserpine effect were studied. Antinociceptive activity was tested using the writhing test. DMI, 10mg/kg s.c.,2 hrs before administration of morphine or aminopyrine, significantly enhanced their antinociceptive activity. Prothiadene, in the same dose and interval before administration of morphine, did not influence the antinociceptive activity of morphine in control mice. It did, however, antagonize the inhibitory effect of reserpine (2.5mg/kg s.c.)on the antinociceptive activity of morphine. Thus, it is possible to detect the antireserpine effect of prothiadene. 3 references.

070949 Podvalova, J.; Dlabac, A. Vyzkumny Ustav pro Farmacii a Biochemii, Kourimska 17, Prague 3, Czechoslovakia Aggressive behavior of rats induced by mesorgydine (Lysenyl SPOFA). *Activitas Nervosa Superior (Praha).* 12(1):81, 1970.

Signs of agitation, vocalization, increased salivation, hostility and sexual manifestations were observed in rats after high doses of mesorgydine. These effects may be regarded as manifestations of aggression because the mode of response closely resembles the expression of fury in normal rats. The inhibitory effect of various drugs on aggressive behavior was tested and it was found that the tranquilizer, chlordiazepoxide and oxazepam, were active in much lower doses than the neuroleptics, chlorpromazine and octoclothepine. The mesorgydine test has possible usefulness for evaluating drugs with potential antineurotic action. 2 references.

070977 Adler, Martin W. Temple University College of Medicine, Philadelphia, Pennsylvania Drug response following brain damage. *In: Smith, W., Drugs and cerebral function.* Springfield, Illinois, Charles C Thomas, 1970. 288 p. (p. 176-186).

Investigation was made of responses to drugs after damage to select areas of the brain, such as the ventromedial hypothalamic nucleus and septal nuclei. In the first group of studies reported, lesions of the ventromedial nucleus in the hypothalamus were found to result in increased food intake; amphetamines inhibited this response. Bilateral ablation of frontal or posterior cortex in rats was found in another study to cause an enhanced response to the effects of amphetamine on locomotor activity. No alterations were noted with cocaine. A third series of experiments involved the production of sham rage reactions by septal nuclei lesions to study effects of various drugs on hyperreactive behavior. The increased sensitivity to pentylenetetrazol in frontally ablated or semidecerebrated cats is also discussed. Careful study of time course of alterations in drug sensitivity, utilizing known anatomical pathways, and searching for biochemical correlates to altered thresholds are approaches suggested in studying pharmacologic action in conjunction with brain damage. 27 references.

070978 Cherkin, Arthur. Psychobiology Research Laboratory, Veterans Administration Hospital, Sepulvada, California Effects of flurothyl on memory processing. *In: Smith, W., Drugs and cerebral function.* Springfield, Illinois, Charles C Thomas, 1970. 288 p. (p. 187-198).

The effect of flurothyl on memory consolidation and amnesic events in chicks is discussed. After pecking at an aversively treated lamp for 10 sec, flurothyl is administered by inhalation for 1, 2, 4, 8 or 16 minutes. Memory retention is tested 20 to 24 hours later by observing whether the chick refuses to peck at a similar but untreated lamp. Retrograde amnesia was found, with a maximum degree at flurothyl concentration of 1.7percent for 8 minutes exposure time. The production of amnesia was dose dependent. The results suggest that amnesia interferes with engram consolidation rather than with retrieval of the engram, although it is possible that both events are affected. The effect of flurothyl upon short term memory and memory retrieval are also discussed. 43 references.

070979 Leaf, Russell C. Rutgers University, New Brunswick, New Jersey Pharmacology, limbic regulation and cortical function. *In: Smith, W., Drugs and cerebral function.* Springfield, Illinois, Charles C Thomas, 1970. 288 p. (p. 201-214).

The selective inhibitory effects of thiazesim on subcortical brain function are discussed. The author used laboratory rats which exhibited mouse killing behavior to study amygdaloid function; it was found that lesions in this region eliminate the mouse killing behavior without depressing other behavior. Amygdaloid injection of antidepressants (imipramine and thiazesim) inhibited mouse killing for up to 3 hours, whereas other drugs lacking antidepressant activity did not. Various indications show that mouse killing is activated by a cholinergic system that may include several subcortical structures. The amygdaloid changes that produce inhibition of mouse killing appear to be associated with an evolved ascending mechanism that causes changes in cortical excitability. Since destruction of the amygdala causes changes in the timing and frequency of a wide range of behaviors, and is not essential for their performance, its function is probablymodulative rather than controlling. Nevertheless, attempts to explain why pharmacological inhibition of mouse killing by rats is related to the antidepressant action of drugs are presently speculative and incomplete. 63 references.

071467 Dasher, Charles E.; Hamilton, Horace E. School of Aerospace Medicine, Brooks AFB, Texas Combined effects of chlorpromazine and altitude upon performance in the rat. Springfield, Va., NTIS, AD-712664. HC$3.00 MF:$.95.

Four male Sprague-Dawley rats were conditioned to press a lever in response to visual and auditory cues, and to release the lever upon termination of the cues. The rodents were then tested under the conditions of saline, chlorpromazine (CPZ), altitude, and CPZ plus altitude. For each set of data, 50 trials of control data were recorded, and then the animals were either injected with saline or CPZ, or, in the case of controls, merely stuck with a needle. Twenty five minutes after injection, an additional 50 trials were recorded. For the altitude data, the rodents were brought to the simulated altitude 5 minutes after injection. Performance was significantly decreased by CPZ (p less than .01) and by altitude (p less than .05), but no CPZ altitude interactions were observed. Saline produced no effect upon performance. (Journal abstract -USGRDR)

071785 Wuttke, Wolfgang. Institut fur Pharmakologie der Farbenfabriken Bayer AG, D-5600 Wuppertal-Elberfeld, Friedrich Ebert-Strasse 217, Germany The effects of d-amphetamine on schedule-controlled water licking in the squirrel monkey. *Psychopharmacologia (Berlin).* 17(1):70-82, 1970.

Three squirrel monkeys performed under a 5 minute fixed interval schedule of food presentation with licking a water filled tube as the required operant response. All subjects developed the characteristic fixed interval pattern of responding: an initial period of little or no responding followed by acceleration of responding to a final rate that is sustained until reinforcement. Over a range of doses, d-amphetamine had a dose related enhancing effect on the overall rate of licking; higher doses decreased the overall rate. Analysis of the effects of d-amphetamine on the different rates within successive 30 second periods of the interval showed that all doses in 1 subject and the higher doses in the 2 others changed the output of the licking behavior in a rate dependent way. Over a range of doses, d-amphetamine not only increased the rate of licking but also the intake of water directly proportional to the number of responses. After high doses, which still increased the rate of responding, the water intake per lick decreased. The effects of d-amphetamine on licking behavior maintained under a fixed interval schedule of food presentation were similar to the effects of amphetamine on other operant responses, such as pressing a lever or pecking a key. Schedule controlled licking is influenced by d-amphetamine differently from drinking which is not under the control of explicit experimental consequences. 18 references. (author abstract modified)

071786 Pradhan, S. N.; Dutta, S. N. Department of Pharmacology, Howard University College of Medicine, Washington, D. C. 20001 Behavioral effects of arecoline in rats. *Psychopharmacologia (Berlin).* 17(1):49-58, 1970.

Effects of arecoline (0.25 to 4mg/kg) were studied on several behavioral schedules in rats, and was found to usually decrease responses (especially at high doses) in schedules including spontaneous motor activity, fixed ratio and fixed interval reinforcement, differential reinforcements of low rates, and shock avoidance. Slight enhancement of responses was observed (at low doses) in spontaneous activity, fixed ratio reinforcement, fixed interval reinforcement and shock avoidance. Arecoline methiodide had negligible and insignificant effects. The depressant effect ofarecoline (2mg/kg) in the spontaneous activity schedule could be antagonized by scopolamine (0.25 and 0.1mg/kg), but not by methylscopolamine (0.5mg/kg), or mecamylamine (2mg/kg). On the other hand, arecoline induced behavioral depression under fixed ratio water and food reinforcement could neither be antagonized by scopolamine (0.25 to 0.1mg/kg), which also caused depression, nor by mecamylamine (2mg/kg). 11 references. (author abstract modified)

071787 Molinengo, L.; Ricci-Gamalero, S. Institute of Pharmacology, Via P. Giuria 13, I-10125 Torino, Italy Action of codeine, pethidine and methadone on the operant behavior of the rat. *Psychopharmacologia (Berlin).* 17(1):34-48, 1970.

In concurrent food reinforced and avoidance schedules, codeine, pethidine and methadone reduced the rate of response by 50 male rats on avoidance and food reinforced levers, reduced the number of avoided shocks at the highest dosages only, and caused variable modifications of the delay. At low doses methadone increased the rate of response. In the 'carried extinction' test, codeine and pethidine reduced the rate of response in all the experimental situations, while in certain cases, methadone had the opposite effect. In conditions of operant inhibition, the inhibitory action of shock was increased by codeine; it was reduced, over a narrow range of doses, by methadone and, less regularly, by

pethidine. The relative analgesic potency of the compounds studied does not correspond to their relative behavioral potency. 20 references. (author abstract modified)

071792 Levinthal, Charles F.; Papsdorf, James D. Psychological Laboratories, 3439 Mason Hall, University of Michigan, Ann Arbor, Michigan 48104 Experimental variables in the effects of postsession injections of strychnine sulphate on a classically conditioned response. ***Psychopharmacologia (Berlin).*** **17(1):100-104, 1970.**

Postsession strychnine injections have been shown to retard acquisition rates of the classically conditioned nictitating membrane response (CCNMR) of 80 to 100 day old rabbits trained at a conditioned stimulus - unconditioned stimulus (CS-US) interval of 1000 msec. The particular interval value employed in CCNMR acquisition was found to beimportant in the magnitude of the postsession strychnine effect. Strychnine subjects trained at a CS-US interval of 1250 msec were significantly depressed in acquisition rates relative to saline controls, while strychnine subjects trained at a CS-US interval of 250 msec were not. Interpretations are based upon the presumed effects of central nervous system excitants on memory consolidation according to the classical conditioning paradigm, and possible neurological correlates of the CS-US interval parameter. 15 references. (author abstract modified)

071997 Phillips, M. I.; Bradley, P. B. Division of Biology, California Institute of Technology, Pasadena, California 91109 Reticular stimulation and chlorpromazine. ***Science.*** **168(3935):1122-1123, 1970.**

Based on the hypothesis that schizophrenics are overaroused as a result of long-term activation of the brainstem reticular formation, Kornetsky and Eliasson proposed that animals electrically stimulated in the reticular formation are overaroused in a similar fashion. They postulated an inverted U model in which overarousal moves subjects beyond an optimum level of performance and chlorpromazine keeps subjects before the optimum point; therefore, the drug reduces the overarousal effects and produces improved performance. Tests with 82 adult male Wistar rats given chlorpromazine and electrical reticular stimulation were conducted. There were fewer errors in performance when intermittent stimulation and chlorpromazine were combined than with either drug or stimulation alone. The effect was more marked with a barbiturate combined with stimulation. It is suggested that where chlorpromazine is most effective, as in confused, hallucinated or agitated patients, there is an impairment in sensory evaluation and chlorpromazine helps to facilitate the process of assessment, rather than alter a state of overarousal per se. 7 references.

072033 Guerrero-Figueroa, R.; Rye, Merrill M.; Gallant, D. M.; Bishop, M. P. Southeast Louisiana Hospital, Mandeville, Louisiana Electrographic and behavioral effects of diazepam during alcohol withdrawal stage in cats. ***Neuropharmacology (Oxford).*** **9(2):143-150, 1970.**

Central nervous system spontaneous and evoked cortical and subcortical activities were evaluated in cats during chronic alcohol administration and following alcohol withdrawal. In the normal and epileptic animals, alcohol was administered through a gastric cannula (Pavlov type) chronically inserted in each cat in the upper quadrant of the greater curvature of the stomach. Chronic alcohol administration produced an increase of EEG fast activity in cortical and subcortical structures associated with suppression of epileptiform discharges and a decrease in the amplitude of the local evoked potentials recorded from cortical and subcortical structures. In contrast, withdrawal from alcohol produced an increase in EEG slow wave background activity associated with activation of epileptiform discharges and an increase in the amplitude of the local evoked potentials recorded from cortical and subcortical structures. In addition, an evaluation of the effects of i.v. and i.p. administration of diazepam is presented. It is concluded that diazepam is an effective drug in the prevention and control of the withdrawal syndrome. Electrical and behavioral studies suggest that chronic alcohol administration has an inhibitory effect upon the integrative action of the CNS, and a reversal of this effect (excitation) occurs during the withdrawal syndrome. Possible mechanisms for such inverse neurophysiological actions are discussed. 19 references. (author abstract)

05 TOXICOLOGY AND SIDE EFFECTS

070821 Smith, Donald F.; Balagura, Saul; Lubran, Myer. Department of Psychology, University of Chicago, Chicago, Illinois 60637 'Antidotal

thirst': a response to intoxication. ***Science.*** **167(3916):297-298, 1970.**

Albino rats increased their water intake after receiving an oral dose of 0.12 molar lithium chloride. The alterations in blood volume and tonicity did not account for the greatly increased thirst, which facilitated the renal excretion of the toxic lithium ions. Antidotal thirst is distinguished from thirst induced by hypovolemia or hyperosmolarity, and is another example of homeostatic mechanism. Thirst occurs as an adverse side effect in manic-depressive patients treated with lithium salt. 8 references.

070906 Pennington, S. N.; Chattopadhyay, S. K.; Brown, H. D. Biochemistry Section, Cancer Research Center, Columbia, Missouri 65201 A possible pathway for ethanol-induced fatty liver and modification of liver injury by antioxidants. ***Quarterly Journal of Studies on Alcohol.*** **31(1):13-19, 1970.**

The roles of acetaldehyde and antioxidants in the metabolism of ethanol were investigated in order to determine the mechanism whereby exposure to ethanol causes a fatty liver condition in rats. The cytochrome P-450 of microsomes incubated in the presence and absence of ethanol, acetaldehyde, and acetaldehyde with alpha-tocopherol was determined spectrophotometrically in calf or rat livers. Ethanol in varying amounts did not change the P-450 concentration but acetaldehyde at varying concentrations linearly lowered P-450 levels from the control level of 32 millimicromoles to approximately 22 at 0.6mg acetaldehyde/3 ml while with the addition of alpha-tocopherol, P-450 levels remained constant at 32 millimicromoles. Apparently acetaldehyde formation from ingested ethanol oxidizes the reduced P-450 so that the oxidation system which normally handles the fatty acids through omega hydroxylation fails to operate, causing a fatty liver. This conclusion is substantiated by the finding that administration of antioxidant prevented the inhibition effect of acetaldehyde on P-450. 23 references.

071993 Ellinwood, E. H., Jr.; Escalante, O. Department of Psychiatry, Duke University Medical Center, Durham, North Carolina Behavior and histopathological findings during chronic methedrine intoxication. ***Biological Psychiatry.*** **2(1):27-39, 1970.**

There is a correlation between the behavior in cats with chronic administration of methedrine and the histopathological findings of catecholamine distribution. Specific behavioral changes associated with chronic amphetamine intoxication in man appear related to changes in arousal systems at several levels in the central nervous system. In acute intoxication, cats demonstrated an inattention to objects in theimmediate environment; they are hyperalert to slight movements or sounds from a distant source, and later develop acute fear responses to any stimuli. With chronic intoxication, a decrease is noted in the above symptoms along with a decrease in tonicity and righting reflexes. The histopathological findings reports a depletion of catecholamine fluorescence in the nerve terminals and neurons located in medial and lateral areas of the brain stem. 24 references. (author abstract modified)

06 METHODS DEVELOPMENT

070063 Fleming, Robert M.; Clark, William G. Veterans Administration Hospital, Sepulveda, Calif. 91343 Quantitative thin-layer chromatographic estimation of labeled dopamine and norepinephrine, their precursors and metabolites. ***Journal of Chromatography.*** **52:305-312, 1970.**

As part of continuing efforts to develop thin layer chromatographic techniques for separation and detection of catechol biogenic amines, a simple quantitative separation method for combinations of 16 C-14 and H-3 labeled catecholamines, their precursors and metabolites was devised. The method uses precoated cellulose plates, diazotized p-nitroaniline as a spray detection agent and quantitates the labeled compounds by means of a liquid scintillation counter. The efficiency of the method was tested by examining differences of in vitro and in vivo metabolism of C-14 labeled dopamine by control and enzyme-inhibited caudate nucleus. 15 references. (Author abstract modified)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

071292 Ralston, John D.; Abreu, Benedict E. Colorado State Division of Corrections, Canon City, Colorado Clinical experience with piperacetazine in hospitalized mental patients: a four year study. *Journal of the Indiana State Medical Association.* 63(11):1291-1296, 1970.

A long-term clinical study to obtain preliminary information on dosage boundaries of piperacetazine, a new psychotherapeutic drug, and to evaluate it is discussed. In a study of 4 years duration, involving 153 hospitalized patients, piperacetazine was judged to be a potent agent for control of agitated, psychotic patients. On a weight basis, 1mg. of oral piperacetazineis generally as effective as 10mg. of chlorpromazine, and in some patients the ratio is even greater. The incidence of side-effects, however, is substantially less with piperacetazine. The average daily maintenance dosage of piperacetazine was 44.7mg.,which is roughly equivalent to 500mg. of chlorpromazine. At this dosage level, side-effects rarely interfered with piperacetazine therapy. The highest daily dosage of piperacetazine (160mg.)could theoretically be the equivalent of 1600mg. or more of chlorpromazine. In certain patients on piperacetazine at such dosage levels extrapyramidalsigns previously induced by chlorpromazine at doses of 400 to 800mg. daily actually disappeared. Therapeutically, piperacetazine and chlorpromazine would appear to differ very little, but the low incidence of side-effects appears to be a notable advantage of the former and permits more intensive medication when needed in the management of patients with chronic mental disorders. Piperacetazine injection (subcutaneous or intramuscular) causes minimal tissue irritation and is highly effective in small dosage. 8 references. (Author abstract modified)

071974 Hofmann, W. W.; Ryan, R. L. Department of Neurology, Veterans Administration Hospital, 3801 Miranda Avenue, Palo Alto, California 94304 A controlled study of L-DOPA in Parkinson's disease. *Arizona Medicine.* 27(2):9-14, 1970.

A small group of patients (23) with Parkinson's disease were treated with oral L-DOPA in order to verify its probable effectiveness. In 10 cases, the drug was administered according to a randomized double-blind crossover protocol and in 13 cases both doctor and patient knew what drug was being administered. During 2 periods of 21 days, the patients were treated with gradually increasing dosages of either lactose or L-DOPA. Each patient was aware that he would be receiving placebo for half of the study. A 1 to 5 day rest was given each patient at the end of the first treatment period. During the last 10 days of each period, the patients were receiving fixed dosages of eight capsules per day (4g). Using a subjective basis, 90% of the patients either improved or were unchanged. The general level of improvement with L-dopa was more than with standard drugs but a combination of these agents was sometimes helpful. Toxic psychosis was a problem in 3 cases but with the exception of nausea, other side-effects were minimal. A beneficial side-effect was the patient's feeling of alertness and well-being. Further study is indicated. 13 references. (author abstract modified)

071984 Wycis, Henry T.; Cunningham, William; Kellett, Garry; Spiegel, Ernest A. Department of Neurosurgery, Temple University Health Sciences Center, Philadelphia, Pennsylvania L-dopa in the treatment of post-surgical Parkinson patients. *Journal of Neurosurgery.* 32(3):281-285, 1970.

In a study of 10 postsurgical and 20 nonsurgical patients, L-dopa (L-dihydroxyphenylalanine) was a valuable drug in the treatment of parkinsonian syndrome, despite side-effects and complications. In 8 of 10 cases previously relieved of tremor and rigidity by stereotaxic surgery, L-dopa therapy improved bradykinesia. Longer periods of observation and careful repeated examination of patients were necessary. The effect of prolonged use is unknown, and the high cost of the drug should also be considered. Surgery is still important in therapy of parkinsonism, particularly in cases with tremor and rigidity unattended by hypokinetic symptoms and unrelieved by medication. 13 references. (author abstract modified)

071985 Stellar, Stanley; Mandell, Stanley; Waltz, Joseph M.; Cooper, Irving S. Department of Neurosurgery, St. Barnabas Hospital, New York, New York L-dopa in the treatment of parkinsonism. A preliminary appraisal. *Journal of Neurosurgery.* 32(3):275-280, 1970.

The discovery that striatal and nigral dopamine is depleted in parkinsonism has indicated that dopamine is probably a true neurotransmitter along a nigro-striatal pathway. Previous clinical investigations have shown that L-dopa (L-dihydroxyphenylalanine), a precursor of dopamine, can alleviate many parkinsonian symptoms. L-dopa does not traverse the blood brain barrier while dopamine does. In a study of 91 patients treated with L-dopa, 75% showed marked or partial improvement. Patients who had previously undergone cryothalamectomy did not do so well. Far advanced, badly disabled patients did least well. Tremor was lessened in a few; rigidity, bradykinesia, facial masking, and voice, gait, and handwriting disturbances were often greatly diminished. A high percentage of patients experienced toxic effects, especially anorexia, nausea, and vomiting. These sometimes occurred with low dosage. Gastrointestinal symptoms gradually subsided in many. Dyskinesias, paranoid ideation, and hypotension were also noted, but all side-effects were reversible, especially if dosage was reduced. The effect of L-dopa on need for surgery is not clarified, but it may obviate the need in some patients and make surgery possible and safer for others. 14 references. (author abstract modified)

072003 Malaguti, Paolo. Via P. Mengoli, 34, 40138 Bologna, Italy /Controlled therapeutic experimentation in cases of psychogenous gastroenteric disturbance./ Sperimentazione terapeutica controllata delle affezioni gastroenteriche ad interferenza psicogena. *Minerva Medica (Torino).* 61(11):479-484, 1970.

Psychogenic gastroenteric disturbances are essentially the result of neurovegetative imbalance linked to the emotions, coupled with functional disturbances of a primarily spastic and hypersecretivenature. With this point in mind, 63 patients were treated with a combination of benzodiazepine and scopolamine methylbromide. The true effectiveness was checked by means of a blind test with an inert placebo and meprobamate. Extremely satisfactory (85.7%) results were obtained, especially in hyperdynamic forms. The new drug was found to decrease the influence of emotive factors without interfering with the subject's normal activities. In this way, the vicious circle between psychic tension and somatic symptoms was broken. 30 references. (author abstract)

072157 Dubois, B.; Balmelle, J.; Fontaine, G. Clinique pediatrique, Cite hospitaliere, 59-Lille, France /Sulpiride in pediatrics./ Interet du sulpiride en pediatrie. *Semaine des Hopitaux de Paris (Paris).* 46(29B):87-92, 1970.

Sulpiride was administered to 56 children aged between 2 months and 15 years suffering from behavior or character disorders of varying origin. The most important group included 35 cases of affective disorders often associated with disturbed family relationships. The effect of sulpiride seemed very valuable when there was an element of depression with apathy and inhibition, social difficulties (e.g. difficulty of group integration), introspection, opposition, extreme dependence on adults, and incontinence. In 11 cases with psychosomatic disorders, such as anorexia or vomiting in young infants without organic cause, sulpiride gave very good results. In infantile psychiatry (5 cases), sulpiride improved social integration, by increasing participation in the life of a group, relieving inhibitions and improving contact. Finally, sulpiride was found to have an excellent effect on abnormal movements, emotional lability and hypotonia in 2 cases of Sydenham's chorea and had a very favorable effect on vigilance, hallucinations, and confusional state in 3 cases on meningo - encephalitis and encephalitis. In all, there were 45 positive results including 17 excellent and 21 good results. The dosage varied between 5 and 10mg/kg/day. The drug was well accepted and tolerated both clinically and according to laboratory tests whatever the duration of treatment. 2 references. (author abstract)

072159 Ropert, R.; Levy, L.; Ropert, M.; Coudiere, G.; Weil, D. Hopital Psychiatrique de Vaucluse, 91-Epinay-sur-Orge, France /Clinical experience of sulpiride in psychiatry./ Notre experience clinique du sulpiride en psychiatrie. *Semaine des Hopitaux de Paris (Paris).* 46(29B):109-116, 1970.

The first of a new chemical family, the substituted benzamides, sulpiride was administered, usually alone, to 72 patients with various mental disorders. Most of them were followed up for 2 years in a psychiatric hospital. The effects of the drug on each group of symptoms are analyzed: the most typical seems to be the effect of disinhibition, and stimulation of certain aspects of mental activity. Sulpiride has practically no sedative effect, which explains why it is not used in

mania and psychomotor agitation. In depressive states, its combination with antidepressors is justified. When used alone, it does not cause true inversion of mood in melancholia; its stimulating and disinhibitory effect is on the other hand useful in depression where it completes the effect of thymoanaleptic drugs, especially as it does not cause side-effects such as asthenia. Side-effects were moderate and the drug is therefore easy to prescribe. (author abstract modified)

072397 Blustein, J.; Rheaume, S.; Sendbuehler, J. M. Department of Psychiatry, The Queen Elizabeth Hospital, Montreal, Canada A pilot study of injectable diazepam in a general hospital setting. ***Laval Medical (Quebec).*** **41(4):490-494, 1970.**

The effect of Valium (diazepam) on 17 patients exhibiting various psychiatric disorders including anxiety neurosis, depression, character disorders, and schizophrenia was investigated. Intramuscular injections of 5 to 10mg were administered every 4 hours for 16 hours to provide a rapid build up of the medication prior to placing the patients on an oral regimen. Diazepam took effect within 15 to 20 minutes. A marked reduction in the intensity of behavioral symptoms began in the first 4 hours and continued throughout the duration of the investigation. There were few adverse effects and Valium Roche injectable was compatible with other medication for nonpsychiatric conditions. Complete hematological, biochemical and hepatic examinations revealed no abnormal findings in any of the patients. 13 references. (author abstract)

08 DRUG TRIALS IN SCHIZOPHRENIA

069795 Skoda, C.; Nestlingerova, E.; Nestarcova, K. Psychiatric Research Institute, Prague-8 (Bohnice), Czechoslovakia Retention rates of schizophrenia: a comparison of shock therapy and psychopharmacological eras and of closed and open door policies. ***Social Psychiatry (Berlin).*** **5(3):172-174, 1970.**

By means of comparison of the retention rates of cohorts of schizophrenic patients admitted to a regional mental hospital at different periods and using neurotic patients as controls, it was found 1) the retention rates were maximal in schizophrenic patients in the shock treatment period and with a closed door policy; 2) retention rates were minimal during the period of psychopharmacotherapy and with the open door system; 3) retention rates during the period of psychopharmacotherapy and closed door policy were distributed between both extremes just mentioned. Corresponding to the marked decrease of bed utilization during the open door system era down to the lowest administratively tolerated degree, a slight nonsignificant elevation of retention rates was observed. In females an interesting but nonsignificant reversal of the trend found for males was observed in the first 3 months of stay. The relation of the subsequent retention rates was similar to that of the male samples, though the only significant difference between cohorts was of greater retention during the closed door period of 1957 in comparison with 1964 during which both the open door system and the psychotropic drugs were in use. The effect on the cohorts of the factors mentioned above, as well as their homogenity in respect to sex, age and clinical diagnosis, may be considered as adequately demonstrated. On the other hand, differences between the cohorts on other parameters that might have influenced the duration of the hospitalization were not analyzed. 10 references. (Author abstract)

069822 Kim, Chang Hwan; Perlstein, Meyer A. Reed-Chicago State Hospital, Chicago, Illinois Encephalitis with catatonic schizophrenic symptoms. ***Illinois Medical Journal.*** **138(5):503-507, 1970.**

A detailed case study is reported of an 8-year-old boy, bitten by a stray dog and given a standard treatment of 14 consecutive daily injections of Semple vaccine (a vaccine grown in the rabbit brain). He developed catatonic schizophrenia characterized by marked personality changes, convulsions, ataxia, muteness and immobility. He was treated with corticosteroids and phenobarbital sodium; chloropromazine was stopped after 3 days because it had no affect on the catatonia. In 6 weeks the child was less withdrawn but still had allalia. The decision to give antirabies vaccine after a bite by a stray animal should be carefully considered since the incidence of lethal reactions to the vaccine is higher than the incidence of rabies from untreated bites. The use of the duck embryo grown vaccine instead of the Semple vaccine is recommended. 44 references.

070880 Hardeman, W. J.; Bakker, S. J. State Mental Hospital, Eindhoven, The Netherlands Double blind comparative study of the effects of thiothixene and thioridazine in twenty chronic

***schizophrenic patients. Psychiatria, Neurologia, Neurochirurgia (Amsterdam).* 73(1):1-7, 1970.**

Twenty chronic schizophrenic males were divided into 2 groups of 10 patients each so that the means of age, evaluability, hospital period and Psychiatrische Universiteits Kliniek (PUK) scale scores in both groups were as equal as possible. (PUK scales are available on request from the Second Psychiatric University Clinic, Aguietenstraat 2, Utrecht, Holland.)An 8 week doubleblind study with thiothixene (42mg/day) and thioridazine (513mg/day) medication failed to produce significant differences in social adjustment as measured by the PUK scales, nor was a significantly different influence exerted on the various subscores of the PUK scales. 16 references. (author abstract modified)

070929 Zapletalek, M.; Rikovsky, S.; Barborakova, E. Neredinska 9, Olomouc, Czechoslovakia Clinical experience with octoclothepine in schizophrenic psychoses. *Activitas Nervosa Superior (Praha).* 12(1):45-46, 1970.

The clinical effectiveness of octoclothepine in 31 cases of schizophrenic psychosis was examined. The patients were clinically examined before and after treatment by the Malamud-Sands Rating Scale, by EEG and by laboratory tests. Dosage ranged from 30-90mg/day for 4 to 5 weeks. Twelve patients were found substantially improved, 14 were improved, 5 showed no change and 1 was worse. The most pronounced effects were on sociability, motor activity, speech improvement, feeling, submissiveness, facial movements and thinking. Minimal improvement was achieved in disturbances of affectivity, mood, appearance and delusions. Side-effects included extrapyramidal symptoms. 3 references.

070930 Rydzynski, Z.; Wierzbicki, T. Ul. Mlynarska Nr. 2, Glowno, Poland Clinical experience with octoclothepin. *Activitas Nervosa Superior (Praha).* 12(1):46-47, 1970.

The administration of octoclothepin as a therapeutic agent to 17 mental patients (15 cases of schizophrenic psychosis, 1 case of involutional depression, 1 case of temporal epilepsy) is reported. The average age of the patients was 43.5-years-old. Most of the schizophrenia was of long duration. Dosage ranged from 5-70mg/day (average, 30.5mg/day). Treatment ranged from 10 days to 4 months. Five patients obtained complete remission; 5 showed evident improvement; 5, little improvement; 2, no improvement; and 4, aggravation of the clinical state. Side-effects included somnolence; decreased blood pressure and extrapyramidal symptoms. Octoclothepin should be subjected to further clinical trials. 2 references.

070931 Nahunek, K.; Rodova, A.; Svestka, J. Psychiatricka Klinika UJEP, Brno, Czechoslovakia /Clinical experience with fluphenazine decanoate./ Klinicke zkusenosti s fluphenazin dekanoatem u psychoz. *Activitas Nervosa Superior (Praha).* 12(1):47-49, 1970.

Fluphenazine decanoate was an effective drug in 80% of schizophrenic patients. The drug was well tolerated; however, parkinsonian symptoms were observed as manifestation of side-effects. Dyskinesia and akathisia were reported. 3 references.

070932 Vencovsky, E.; Sedivec, V.; Peterova, E.; Baudis, P.; Dvorakova, M. Psychiatricka Klinika LF KU Dukelska 69, Plzen, Czechoslovakia /Clinical experience with fluphenazine-depot./ Klinische Erfahrungen mit fluphenazin-Depot. *Activitas Nervosa Superior (Praha).* 12(1):49-50, 1970.

The effects of per os and depot injections of Fluphenazine-Depot were examined in 41 schizophrenic patients. Therapeutic effects of the drug were observed in 50% of the patients. Side effects consisted of akathisia, tremor and hypokinetic - hypertonic syndrome.

070935 Nahunek, K.; Hadlik, J.; Rodova, A.; Misurec, J.; Vanysek, J. Psychiatricka Klinika UJEP, Brno, Czechoslovakia /A comparison of triperidol and perphenazine in schizophrenia. Effects on myoclonic threshold./ Srovnani triperidolu s perphenazinem u schizofrennich psychoz. Vliv na fotomyoklonicky prah. *Activitas Nervosa Superior (Praha).* 12(1):56,57, 1970.

A double-blind study of the therapeutic effects of triperidol and perphenazine was carried out on 36 patients with diagnoses of schizophrenia and paraphrenic psychosis. Clinical and biochemical parameters as well as EEG's and an evaluation of photomyoclonic thresholds were performed during the therapy. The results revealed the good therapeutic properties of both triperidol and perphenazine in the treatment of schizophrenia. Perphenazine was more effective in the first weeks of therapy against aggressiveness and improved insomnia. Triperidol, on the other hand, was most effective in cases of decreased motor

activity. No hepato- or nephrotoxicity was found. 3 references.

070936 Svestka, A.; Nahunek, K. Psychiatricka Klinika UJEP, Brno, Czechoslovakia /A comparison of the effects of methylperidol and perphenazine in schizophrenic psychosis./ Kontrolovane stovnani metylperidolu s perfenazinem u psychoz schizofrenniho okruhu. *Activitas Nervosa Superior (Praha).* 12(1):57-58, 1970.

The therapeutic effects of methylperidol and perphenazine were studied in 31 female patients with schizophrenic psychoses. Perphenazine possessed a broader spectrum of therapeutic effects, marked by the effective abolishment of many pathological symptoms. Parkinsonian symptoms and oral dyskinesis were reported as side-effects of both drugs.

070938 Hadlik, J.; Svestka, J.; Nahunek, K.; Rodova, A. Psychiatricka Klinika UJEP, Brno, Czechoslovakia /A controlled study of the effect of thiothixene and perphenazine in psychoses and schizophrenia./ Kontrolovana studie s thiothixenem a perfrenazinem u psychoz schizofrenniho okruhu. *Activitas Nervosa Superior (Praha).* 12(1):60-61, 1970.

Thiothixene and perphenazine were administered to 21 patients with psychosis, 13 patients with paranoid schizophrenia, 5 patients with paraphrenia and to 1 patient with schizoaffective psychosis. Both thiothixene and perphenazine possess beneficial effects on patients with psychosis; the former had more positive effects on sleep, mood, self-evaluation, sociability, anxiety, aggressivity and hallucination. The study revealed the therapeutic value of both of the above mentioned neuroleptics in the therapy of psychoses and schizophrenia. 3 references.

070950 Nahunek, K.; Svestka, A.; Rodova, A.; Novotna, D. Psychiatricka Klinika UJEP, Brno, Czechoslovakia /Occurrence of periodic psychoses during prophylactic administration of lithium./ Vyskyt recidiv u psychoz pri profylakticke lithioterapii. *Activitas Nervosa Superior (Praha).* 12(1):82-83, 1970.

Patients with manic-depressive syndrome, paraphrenic psychoseswere prophylactically treated with lithium salts. During the short time of lithium therapy, relapses were observed in 39% of the manic -depressive patients. In the group of schizophrenics, relapses were observed in 77% of the cases. 3 references.

071322 May, Philip R. A.; Tuma, A. Hussain. University of California at Los Angeles, Los Angeles, Calif. 90024 Methodological problems in psychotherapy research: observations on the Karon-VandenBos study of psychotherapy and drugs in schizophrenia. *British Journal of Psychiatry (London).* 117(540):569-570, 1970.

A review of a note by Karon and VandenBos claiming that additional psychotherapy of schizophrenic patients produced significantly better results than the usual hospital treatment finds so many grave deficiencies in methodology that their conclusions are virtually nullified. Their results are contrary to the general trend in other studies, which indicate that psychotherapy for hospitalized schizophrenic patients is relatively ineffective while drug therapy enhances results, regardless of the therapist's experience. Among faults found in the Karon study are the facts that: 1) the sample size was too small; 2) 3 of the 11 patients in the group supposed to be treated with psychotherapy alone were given antipsychotic drugs; 3) the validity of the diagnosis in 3 patients is questionable; and 4) the 'control group' is not carefully maintained. 1 reference.

072142 Villeneuve, C.; Ananth, J. V.; Ban, T. A.; Lehmann, H. E. Douglas Hospital, Verdun, Quebec, Canada CI-601, a butyrophenone derivative, in the treatment of chronically withdrawn schizophrenic patients. *Current Therapeutic Research.* 12(4):223-229, 1970.

In a double-blind, 10 week controlled clinical study, CI-601, a new butyrophenone compound, was found to be comparable in overall therapeutic effectiveness to haloperidol, a standard butyrophenone drug. CI-601 was found to be especially effective in relieving emotional withdrawal and hallucinatory behavior, suggesting its usefulness in the treatment of chronic withdrawn schizophrenic patients. 5 references. (author abstract)

072144 Zimmermann, Robert L.; Vestre, Norris D.; Schiele, Burtrum C.; Curran, John. University of Minnesota, Minneapolis, Minnesota A controlled study of the effects of gamfexine in phenothiazine-treated patients. *Current Therapeutic Research.* 12(4):230-233, 1970.

Seven chronically anergic schizophrenic patients, who had shown favorable responses to gamfexine plus thioridazine in a pilot study, were selected for a double-blind comparison of gamfexine plus thioridazine versus placebo plus

thioridazine. A modified crossover design was used in which each patient had 5 two week trials on each treatment condition. Ratings of psychopathology were made by the psychiatrist and by nurses prior to the start of medications and at the end of each 2 week treatment period. During the periods when gamfexine was added to the thioridazine, the patients were rated significantly higher on irritability and lower on neatness. However, since a total of 36 variables were analyzed, these 2 significant differences could be attributed to chance. Patients showed significantly lower standing systolic blood pressures and higher pulse rates during the periods when gamfexine was administered. Thus, despite physiological evidence of drug activity, no consistent accompanying behavioral effects were observed. 5 references. (author abstract)

072145 Sugerman, A. Arthur; Herrmann, Jane; O'Hara, Mary. New Jersey Bureau of Research in Neurology and Psychiatry, Princeton, New Jersey A pilot study of AHR-1900 in chronic schizophrenic patients. *Current Therapeutic Research.* 12(4):234-236, 1970.

AHR-1900 was given to 13 male chronic schizophrenic patients, of whom 10 had doses up to 300mg daily, 2 of the others having maintenance doses reaching a maximum of 225mg daily, and the last patient having 25mg daily only. The study was concluded after 60 days of drug administration following an initial placebo period of 24 days. Globalratings showed no unequivocal evidence of antipsychotic activity, most patients showing worsening. Psychiatric and nursing rating scales showed no significant changes. The major side-effect was hypotension. No significant changes were seen in electrocardiogram, electroencephalogram and laboratory examination. At doses up to 300mg daily, the drug appears to lack efficacy in the treatment of chronic schizophrenic patients. 2 references. (author abstract)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

070287 Lewis, Wade H.; Suris, Orlando R. Dept. of Psychiatry, Santa Rosa Medical Center, P. O. Box 7330, Station A, San Antonio, Tex. 78207 Treatment with lithium carbonate: results in 35 cases. *Texas Medicine.* 66(12):58-63, 1970.

Treatment of 35 hospitalized manic and schizoaffective patients with lithium carbonate over a 6 to 12 month period was evaluated. Therapeutic results were termed excellent in 17 patients, good in 10, bad in 5 and needed further observation in 3 other cases. Side effects were minimal and occurred early in therapy. All of the patients accurately diagnosed as manic-depressive responded with almost immediate remission of symptoms when therapeutic blood levels were obtained. Some schizoaffective schiophrenics also showed improvement when lithium carbonate was augmented with a phenothiazine. It was concluded that hospitalization is essential for the establishment of a tailored dose. 10 references.

070856 Damasio, Antonio R.; Antunes, J. Lobo; Macedo, Carlos. Department of Neurology, Hospitais Civis de Lisboa, Lisbon, Portugal L-dopa, parkinsonism, and depression. *Lancet (London).* 2(7673):611-612, 1970.

In a letter to the editor, the authors report a study of the psychologic effects of L-dopa on parkinsonism patients. Thirty patients participated in a trial which included psychometric evaluation in the hospital, and weekly scoring on multi-item rating scales. Depression was diagnosed in 13 patients. These cases were separated, according to etiology, into the following groups: (1) reactive depression (5 patients); (2) endogenous depression (5); (3) organic depression (2); (4) symptomatic depression (1). In 5 patients, depressive symptoms worsened; the others either improved or remained the same. The grouping of depressive syndromes according to major diagnostic divisions may be of importance because clinical picture, prognosis, and response to treatment vary depending on whether depression is mainly reactive, mainly organic, or mainly endogenous. It is suggested that L-dopa changes the clinical picture of endogenous depression, the change resembling that induced by drugs causing 'pharmacogenous psychopathological syndromes' such as neuroleptics, tuberculostatics and corticosteroids. Disturbances associated with L-dopa seem to be independent of dose. 1 reference.

070857 van Praag, H. M.; Korf, J. Psychiatric Clinic, State University of Groningen, Groningen, The Netherlands L-tryptophan in depression. *Lancet (London).* 2(7673):612, 1970.

In a letter to the editor, the author advances an explanation for the observed discrepancy between results of investigations into the antidepressant properties of L-tryptophan. It is noted that

probenecid inhibits the transport of 5-hydroxy indoleacetic acid (5-HIAA) from the brain and cerebrospinal fluid (CSF) to the bloodstream. A study is reported in which 14 patients with 'vital' depression and 11 nondepressive controls were used. In all subjects in both groups, the 5-HIAA concentration in the CSF rose after probenecid; however, the increase in the depression group was significantly less than that in the control group. These findings support the hypothesis of a causal connection between depression and 5-hydroxytryptamine (of which 5-HIAA is the principal metabolite.)However, disorders of 5-HT metabolismwere not found in all depressed patients; 7 subjects did not show increased 5-HIAA in the CSF to an important degree. It is hypothesized that the effect of depression of L-tryptophan is an expression of the fact that L-tryptophan is less effective in patients in whom the probenecid effect of 5-HT metabolism is within normal limits. In patients with a subnormal probenecid effect, L-tryptophan is effective. 9 references.

070927 Nahunek, K.; Svestka, J.; Rodova, A. Psychiatricka Klinika UJEP, Brno, Czechoslovakia /Clinical experience with octoclothepine in manic syndromes./ Klinicka zkouska s octoclothepinem u manickych syndromu. ***Activitas Nervosa Superior (Praha).*** **12(1):44, 1970.**

The therapeutic effects of octoclothepine were studied in patients with manic states. Octoclothepine was administered per os in a dose of 10-40mg/day. The drug had an significant effect on sleep; changes from hypopolarity to hyperpolarity were observed. Parkinson symptoms were found as manifestations on side-effects. No signs of hepato-, hemo-, or nefrotoxicity were noted. 3 references.

070928 Svestka, J.; Nehunek, K. Psychiatricka Klinika UJEP, Brno, Czechoslovakia /Long-term treatment with octoclothepine -- side-effects and laboratory findings. Dlouhodobe podavani Octoclothepinu u psychoz -- sledovani biologickych parametru. ***Activitas Nervosa Superior (Praha).*** **12(1):45, 1970.**

Octoclothepine was administered to 30 patients with psychosis. The relapse of psychosis was observed in only 7%of the cases after long-term therapy. Transient shifts in hepatograms were observed in the patients with histories of chronic hepatitis. 3 references.

070937 Vencovsky, E.; Peterova, E.; Baudis, P.; Dvorakova, M. Psychiatricka Klinika LF UK, Dukelska 69, Plzen, Czechoslovakia /Clinical use of thiopropazate (Dartalan) in patients with psychosis./ Anwendung von Thiopropazat (Dartalan) bei psychotischen Kranken. ***Activitas Nervosa Superior (Praha).*** **12(1):59-60, 1970.**

Dartalan (thiopropazate) was administered to a group of 12 psychotic patients in a dose of 53mg daily for 25 days. Apathy and mutism were completely abolished in all patients studied; of Dartalan was lesseffective in hallucinatory and paranoid syndromes.

070939 Zapletalek, M.; Rikovsky, S.; Mrna, B.; Koluch, J. Neredinska 9, Olomouc, Czechoslovakia Clinical pilot study of dibenzepine treatment of depression. ***Activitas Nervosa Superior (Praha).*** **12(1):61-62, 1970.**

A clinical pilot study of dibenzepine (Noveril) in the treatment of depression was made on 15 patients (5 with depressive neuroses, 10 with depressive psychoses). The average age of the patients was 43.5-years-old. Noveril was given in a daily dose of 240-500mg for 30 days. A rating scale for depressive states was administered before treatment, after the first week of therapy and at the end of treatment. EEGs and tests of physiological function were conducted. Noveril produced a significant improvement of anxiety, speech, interest in environment, concentration, mood and motor activity as well as of contact with environment, suicidal intentions and lack of interest in food. Noveril had no effect on EEG and laboratory tests. Side -effects included sweating and insomnia. 5 references.

070940 Nahunek, K.; Hadlik, J.; Svestka, J.; Rodova, A.; Misurec, J. Psychiatricka Klinika UJEP, Brno, Czechoslovakia /The clinical testing of hydrothiadene in endogenous depressions. Influence of drugs on photomyoclonic threshold./ Klinicka zkouska s hydrothiadenem u endogennich depresi. Vliv na fotomyoklonicky prah. ***Activitas Nervosa Superior (Praha).*** **12(1):62-63, 1970.**

Twenty eight patients with endogenous or involutional depressions were given 25mg of hydrothiadene per os. Therapy was completed with barbiturates or glutethimide. The onset of therapeutic effect was observed in the eleventh day of therapy. Good tolerance of the drug was found in all of the cases. Side-effects of hydrothiadene were not observed. 5 references.

070941 Svestka, J.; Nahunek, K. Psychiatricka Klinika UJEP, Brno, Czechoslovakia /Tranylcypromine in the therapy of endogenous depressions./ Tranylcypromin v lecbe endogennich depresi. *Activitas Nervosa Superior (Praha).* 12(1):63-64, 1970.

The antidepressive effect of tranylcypromine was studied in 33 women with endogenous depression, involutional melancholia and manic - depressive syndrome. Tranylcypromine was found effective in 42.4% of the cases; Full remission was achieved. In 18% of the patients,hypomania, paranoia and hallucination were reported as a result of the therapy. 5 references.

070942 Nahunek, K.; Svestka, J.; Rodova, A. Psychiatricka Klinika UJEP, Brno, Czechoslovakia /Clinical experiences with chlorimipramine in endogenous depression./ Klinicke zkusenosti s chlorimipraminem u endogennich depresi. *Activitas Nervosa Superior (Praha).* 12(1):64-65, 1970.

In 36 patients with endogenous involutional psychoses, chlorimipramine was administered daily in a dose of 165mg together with barbiturates and glutethimide for 25 days. Chlorimipramine appeared to be more effective in depressive forms of psychoses than in other types of psychoses. In the group of patients with anxiety and atypical forms, chlorimipramine was effective in 50% of the cases. The antidepressant index of chlorimipramine was found to be very close to 1.97. Chlorimipramine represents an effective antidepressant with imipramine like therapeutic properties. 3 references.

070943 Rodova, A.; Svestka, J.; Nahunek, K. Psychiatricka Klinika lek. fak. UJEP, Brno, Czechoslovakia /Clinical experiences with desimipramine in endogenous and involutional depressions./ Klinicke zkusenosti s desipraminem u endogennich a involucnich depresi. *Activitas Nervosa Superior (Praha).* 12(1):65-66, 1970.

In 55 patients with periodic endogenous depression, manic depressive syndrome, insomnia, and involutional depression, desimipramine was administered in a dose of 200-250mg. Positive results were achieved in 45.5% of the cases. The therapeutic effect occurred approximately 8 days after the start of therapy. 5 references.

070944 Rydzynski, Z.; Weychert, A. Ul. Mlynarska Nr. 2, Glowno, Poland Value of amitriptylin - spofa in the psychiatric out-and inpatient practice. *Activitas Nervosa Superior (Praha).* 12(1):67, 1970.

The therapeutic effects of amitriptyline were compared with the effects of other thymoanaleptic drugs. The efficacy of the drugs was tested in 15 cases of depression with nocturnal enuresis and also in 16 children with enuresis. The patients with reactive depression and emotional depression responded to therapy with amitriptyline; the beneficial effect of the drug was mainly directed at anxiety, tension, insomnia and agitation. Amitriptyline Spofa is an effective thymoanaleptic drug, which can also be used in the treatment of nocturnal enuresis.

070952 Bily, J.; Groh, J.; Hametova, M.; Hanus, H.; Hrubecka, J.; Polackova, J.; Preiningerova, O. Psychiatricka Klinika LF, Hradec Kralove, Czechoslovakia /Some exeriences with a preventive administration of lithium salts in manic-melancholic psychosis./ Nektere zkusenosti s preventivnim podavanim lithiovych soli u maniomelancholicke psychozy. *Activitas Nervosa Superior (Praha).* 12(1):86-87, 1970.

Twenty one patients with manic-melancholic psychosis were subjected to chronic lithium therapy. A dose of 0.3-1g was necessary to achieve an effective serum level of 0.60 to 1.00meq/l in the patients. The depression symptoms were found to have less significance in the lithium treated patients. The significance of lithium in the therapy of depressions is discussed. 4 references.

070956 Nahunek, K. Psychiatricka Klinika UJEP, Brno, Czechoslovakia /Actual problems of endogenous and exogenous depressions./ K nekterym aktualnim problemum endogenni deprese. *Activitas Nervosa Superior (Praha).* 12(1):93-95, 1970.

The antidepressant effects of electroshock and psychopharmacological therapy were compared. A broad spectrum of antidepressant effects was observed after electroshock therapy. This form of therapy was effective in all types of depression examined in this study. Among the psychopharmacologic drugs tested the highest therapeutic effect was found after amitriptyline. Imipramine was found effective in 60% of the patients, nortriptyline in 77.4% of the cases, melitracene in 58%, and northiadene in 60%. In anxiety, agitation and atypic forms of depression fluphenazine, levopromazine, thioridazine and chlorpromazine were effective.

071043 Trice, John. 150 Talmadge Drive, Athens, Georgia Chemotherapy in private psychiatric practice. *Journal of the Medical Association of Georgia.* 59(9):365-368, 1970.

Promising results are obtained from thioridazine treatment of ambulant mental patients. Thioridazine treatment is even more effective when employed in conjunction with psychotherapy, to facilitate patient psychiatrist communication. Thirty-eight patients (19 male, 19 female; 18 to 80 years of age; 25 showing schizophrenic reaction), all with anxiety and nervous tension which affected the patient's functioning within the community, were treated with thioridazine for periods ranging from 1 week to more than 1 year. Symptoms of anxiety, nervous tension, apprehension, and restlessness; and psychotic manifestations such as delirium, hallucinations, crying spells, and confused states; were significantly improved. Thioridazine was well tolerated, sidereactions were mild and transient, with desirable absence of interference with the patient's alertness. 6 references.

072055 Porter, A. M. W. Camberley, Surrey, England Depressive illness in a general practice. A demographic study and a controlled trial of imipramine. *British Medical Journal (London).* No. 5699:773-778, 1970.

The distribution of 93 consecutive cases of depressive illness in a Surrey general practice was found to be non-random. Married women were at risk, while men and unmarried women were largely spared from this illness. Married women were prone to the disorder at any time in their lives, and relapse was frequent. There was some suggestion that divorced wives and wives of low social class were particularly predisposed to the disorder. Sixty of the patients took part in a double-blind controlled trial of imipramine. There was no evidence that the drug was superior to a placebo in inducing a remission. It is suggested that imipramine has become established in clinical practice on inadequate evidence and that there is a need for further trials.

072381 Schutz, E. Weinmarkt, 8804 Dinkelsbuhl, Germany /Treatment of psychosomatic disturbances associated with psychic symptoms in internal medicine by means of Doxepin./ Die Behandlung psychosomatischer Storungen und psychischer Begleitsymptome innerer Erkrankungen mit Doxepin. *Medizinische Welt (Stuttgart).* 21(31/32):1391-1394, 1970.

Doxepin (dibenzoxepine), a thymoleptic, was tested in a group of patients with various types of depression or psychovegetative disorders with somatic manifestations. The average effective dosage was found to be 16mg/day in the 127 (104 women, 23 men) patients, with the optimal dosage level varying in individuals. The testing was carried out over a period of 24 months and was found to have good sedating, antianxiety and soporific action in patients with abnormal psychic reactions in the course of vegetative disturbances and organic neuroses. Side-effects were not encountered; the drug is recommended for use in daily practice with ambulant patients suffering from psychosomatic disturbances. 13 references. (author abstract modified)

10 DRUG TRIALS IN NEUROSES

070288 Golden, Richard L. Huntington Hospital, Huntington, New York Prevention of paroxysmal tachycardia of Wolff-Parkinson-White syndrome with combined propranolol and quinidine therapy. *Psychosomatics.* 11(6):585-586, 1970.

A 29 year old man with Wolff Parkinson White syndrome was successfully treated for the prevention of recurrent supraventricular tachycardia with a combined propranolol and quinidine regimen. The use of propranolol and quinidine may produce a synergistic effect, and warrants further therapeutic trial. 10 references. (Author abstract)

070946 Zapletalek, M.; Lisonkova, D.; Capakova, L. Neredinska 9, Olomouc, Czechoslovakia Amitriptyline, chlorprothixene, prothiadene and placebo in the treatment of neuroses. *Activitas Nervosa Superior (Praha).* 12(1):70, 1970.

A double-blind crossover study of amitriptyline, chlorprothixene, prothiadene and placebo was conducted on 24 neurotic outpatients. The patients, average age 40-years-old, were evaluated clinically and with the use of a neurotic and autonomic symptoms rating scale before and on the sixth day of treatment. Amitriptyline (10mg/tablet), chlorprothixene (5mg/tablet) and prothiadene (25mg/tablet) were administered for 5 days. The symptoms examined were: depression or anxiety, fatigue and exhaustion, irritability and excitability, emotional lability with tearfulness and the feeling of insecurity. All drugs showed a pronounced effect on the patients' initial condition. Chlorprothixene and prothiadene ameliorated irritability and excitement while prothiadene and

placebo were more effective on mood. Other differences were noted, however, none were statistically proved by an analysis of variance. None of the 21 symptoms were found to be significantly affected by any of the drugs in comparison with the placebo. 2 references.

072140 Sterlin, C.; Ban, T. A.; Lehmann, H. E.; Jarrold, Louise. Hospital des Laurentides, Verdun, Canada A comparative evaluation of doxepin and chlordiazepoxide in the treatment of psychoneurotic outpatients. *Current Therapeutic Research.* 12(4):195-200, 1970.

Thirty psychoneurotic outpatients were randomly divided into two groups and given either doxepin or chlordiazepoxide in a double-blind study. Convariance analyses failed to produce statistically significant results; however, an analysis of the individual symptoms revealed significant improvement with both drugs. In particular, doxepin effected significant improvement on anxiety, tension, somatic concern, guilt feelings, depressive mood, and motor retardation on the brief psychiatric rating scale, and chlordiazepoxide effected significant improvement on anxiety, tension, guilt feelings and depressive mood. Drowsiness and dizziness were prominent side-effects noted in both groups; other side-effects were infrequent, and there were no abnormal laboratory findings. Apparently doxepin and chlordiazepoxide are equally effective in the treatment of psychoneurotic reactions. Doxepin may have a more favorable effect in cases of anxiety associated with depression. 8 references. (author abstract)

072141 Simeon, Jovan; Spero, Monroe; Nikolovski, Oliver T.; Fink, Max. Division of Biological Psychiatry, Department of Psychiatry, New York Medical College, New York, New York A comparison of doxepin and chlordiazepoxide in the therapy of anxiety. *Current Therapeutic Research.* 12(4):201-212, 1970.

Of 43 ambulatory patients in a community mental health clinic with predominant symptoms of anxiety treated with doxepin or chlordiazepoxide, 10 patients received placebo only. Of 19 patients who received doxepin, 75 to 250mg daily, 12 completed 8 or more weeks of treatment. Improvement was marked in 5 patients, moderate in 5, and slight or none in 2. Sixteen patients were treated with chlordiazepoxide and 9 completed 8 or more weeks of treatment. Maximum dosage was 200mg daily. Improvement was marked in 1 patient, moderate in 3, and slight or none in 5. Secondary symptoms with doxepin were minimal except for complaints of dizziness in 4 patients, and drowsiness, dry mouth and constipation in two. In analyses of individual items of behavioral scales, doxepin exhibited reductions of anxiety and depression greater than with chlordiazepoxide. The clinical application of doxepin is seen to be in the therapy of anxiety and depressive symptoms, and this is consistent with the electroencephalographic profiles established in studies in normal volunteers. 27 references. (author abstract modified)

072143 Kingstone, E.; Kolivakis, T.; Kossatz, I. Department of Psychiatry, McGill University, Montreal, Quebec, Canada Doxepin versus chlordiazepoxide: a double-blind study on anxious outpatients. *Current Therapeutic Research.* 12(4):213-222, 1970.

Thirty patients with symptoms of anxiety were randomly divided into 2 groups and given either doxepin or chlordiazepoxide in a double-blind manner. Though the Institute for Personality and Ability Testing and Buss-Durkee Hostility Inventory failed to show any significant differences between the pre- and posttreatment and between the effects of the 2 drugs, the Global Assessment showed that 9 out of 15 patients in each group improved while taking their medication. Dryness of the mouth caused by doxepin was the only significant side-effect. Methodological problems are discussed. Doxepin and chlordiazepoxide appear to be interchangeable in the treatment of anxious patients. 14 references. (author abstract)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

070476 Rasmussen, O. Steen. Asylvej 54, 8240 Risskov, Denmark Fluphenazine enanthate in sesame oil, a depot preparation. *Acta Psychiatrica Scandinavica (Kobenhavn).* 46(3):311-318, 1970.

A trial of fluphenazine enanthate, a depot phenothiazine given by injection every 2 to 4 weeks, is described. A study in 32 acutely relapsing psychotic female patients was carried out. Twelve patients have now been on the drug for 12 to 36 months with a mean of 22 months. Only 1 patient relapsed and required readmission on 3 occasions. Fluphenazine enanthate is, therefore, an important and useful new preparation for

a group of patients who are unreliable at taking oral neuroleptics. Unfortunately, the preparation produced a high occurrence of extrapyramidal effects and in 10 or the original 32 cases the drug had to be stopped for this reason. 14 references. (Author abstract)

071123 Kerr, M. Mck. Christchurch, New Zealand Amitriptyline in emotional states at the menopause. ***New Zealand Medical Journal (Dunedin, New Zealand).*** **72(461):243-245, 1970.**

Fifty patients with emotional states associated with the menopause were included in a double-blind study of amitriptyline (Tryptanol) versus placebo. The results showed conclusively the antidepressant and the antianxiety effect of amitriptyline. Associated symptoms such as insomnia, headache, apathy, fatigue and palpitation also improved markedly with amitriptyline. 5 references. (journal abstract)

071946 Alderton, Harvey R. Thistletown Regional Centre, 1800 Islington Avenue West, Rexdale, Ontario, Canada Imipramine in childhood enuresis: further studies on the relationship of time of administration to effect. ***Canadian Medical Association Journal (Toronto).*** **102(11):1179-1180, 1970.**

Previous studies have shown that imipramine administered at 8 p.m. had its greatest effects on enuretic incidents occurring after 1 a.m. The relation of time of administration of a single maximal dose (50mg) to time of enuresis was studied. The subjects included 8 boys and 1 girl, from 7 to 10 years of age, who were admitted for serious acting out behavior disorders. The results indicated that the 50mg dose produced blood levels which were sustained long enough to control enuresis over a long time span and no advantage was obtained by relating time of administration to time of enuresis. 2 references.

072146 Beaubien, J.; Ban, T. A.; Lehman, H. E.; Jarrold, Louise. Douglas Hospital, Verdun, Canada Doxepin in the treatment of psychoneurotic patients. ***Current Therapeutic Research.*** **12(4):192-194, 1970.**

Doxepin and chlordiazepoxide were compared for their therapeutic effectiveness in a 4 week clinical study of 30 psychoneurotic patients. A flexible dosage schedule was followed: the minimum and maximum daily doses were 75 to 150mg of doxepin and 30 to 60mg of chlordiazepoxide, respectively. No meaningful differences between the range of therapeutic activity of the 2 treatment regimens were found. The improvement in anxiety with doxepin was associated with an improvement of depressive mood, and the improvement of anxiety with chlordiazepoxide was associated with an improvement of tension. 7 references. (author abstract modified)

072158 Robert, G.; Mercier, J. Hopital Psychiatrique, 22-Plouguernevel, France /Sulpiride in psychiatric treatment: clinical and psychometric study in 58 patients./ Le sulpiride en therapeutique psychiatrique: etude clinique et psychometrique chez 58 malades. ***Semaine des Hopitaux des Paris (Paris).*** **46(29B):124-132, 1970.**

A varied sample of neurotic and psychotic subjects was submitted to psychometric assessment initially unmodified and again 5 months after treatment with sulpiride alone. Wittenborn's scale, which permits one to measure the intensity of psychiatric symptoms, was used and completed in some cases by the Rorschach, T.A.T., Minnesota Multiphasic Personality Inventory, and Wechsler tests. Both types of clinical and psychological analysis enable one to study in greater detail the various effects of sulpiride. The term polypsychotrope is used for its anxiolytic effect, its restoration of vitality, mood stimulation, sensation of feeling better, and lifting of inhibitions. Among the 3 main areas in which favorable results for sulpiride were obtained include: chronic confusional states, deficiency syndromes, and sequelae of cranial trauma. (author abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

070415 Darrah, Guard. Preston School of Industry, California Youth Authority, Sacramento, California Some dope users speak out. ***Youth Authority Quarterly.*** **23(2):9-15, 1970.**

The comments of 5 wards at the California Youth Authority's Preston School of Industry provide some insight into the reasons a young person takes drugs and his experiences when he takes them. Similar drugs produce similar feelings. Those who have taken LSD report ecstatic, mystical experiences, while heroin users are less evangelical and less vital to talk to. Two of the young men had taken LSD, one had sniffed some glue and taken some heroin but was not an addict, while one liked cocaine and one was frankly a

heroin addict who could hardly wait to get back to the drug. One of the LSD users pointed out that no efforts were made to convince him that taking drugs was wrong, but he was taught fear of being caught and punished.

070954 Marecek, P.; Bakalar, E.; Janatka, J. Ustredni Vojenska Nemocnice, Prague-Stresovice, Czechoslovakia /The influence of long-term premedication with tranylcypromine on experimental psychoses induced by LSD./ Vliv 21 denni premedikace tranylcyprominem na obraz experimentalni psychozy LSD. *Activitas Nervosa Superior (Praha).* 12(1):90-91, 1970.

In 5 volunteers, the influence of tranylcypromine on the psychotomimetic effect of LSD was studied. Tranylcypromine was administered in a dose of 20mg per day. Chronic premedication with tranylcypromine significantly decreased the effect of LSD. The clinical picture of intoxication was reported to be similar to alcoholic intoxication.

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

069802 Sylvester, John D. Biddulph Mansions, Elgin Avenue, London, W. 9, England The concept of the 'visual computer' and its exploration by the use of drugs. *Studia Psychologica (Bratislava, Czechoslovakia).* 12(3):227-237, 1970.

A cybernetic theory of visual perception is presented to account for experimental results described here together with other known data of perception, particularly adaptation, and with the known functions of the reticular formation of the brain. The theory describes details of higher cortical processes and accounts for the connection between personality differences and individual differences in perception. Two experiments are described, using a combination of cue reduction and drugs to investigate directly the hypothesis put forward. The results of the experiments show that size constancy, in conditions of cue reduction, is diminished by sodium amytal, a depressant drug. The drug may produce the effect either by reducing the physiological cues arriving at the cortex or by reducing the efficiency of the cortical analyzer, the processes of calculation of, or compensation for, distance. Shape constancy is equally reduced by the depressant drug. The suggestion here is that it is the previously learned associations between retinal shape, tilt and real shape which are being interfered with. Probabilities seem to be on the side of a reduction of efficiency of the perceptual computer rather than on reduction of physiological cues, but experiment is not conclusive. However, both experiments strongly support the concept of a visual computer put forward in the discussion. 22 references. (Author abstract modified)

069852 Chase, Thomas N. Unit on Neurology, Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland Biochemical and pharmacologic studies of dystonia. *Neurology.* 20(11):122-130, 1970.

The diversity of response to L-dopa in patients with dystonia is discussed. One patient who changed dramatically was younger and had had the clinically manifested illness for a shorter time than patients in whom the drug was used without effect. He also had a positive family history of dystonia. It is concluded that some patients manifesting torsion dystonia may be substantially improved by L-dopa. The biochemical defect in these individuals as well as the mode of action of L-dopa require study. A discussion of the research on the subject is included. It is important to distinguish between genuine cases of dystonia and cases that are hysterical in origin. 27 references.

070021 Joseph, Herman; Dole, Vincent P. Office of Probation, Manhattan Supervision Branch, Criminal Courts of New York City, New York, N. Y. Methadone patients on probation and parole. *Federal Probation.* 34(2):42-48, 1970.

The methadone maintenance program, started as a research project in 1964 by the Health Research Council of New York City, is an evaluated medical counseling treatment capable of salvaging previously intractable, hard core heroin addicts. Methadone appeases the narcotic hunger generated by opiate abuse that appears to be symptomatic of a metabolic change in the nervous system. Methadone, administered once daily by mouth, in constant dose, acts as a normalizer and permits the patient to function as a normal individual with none of the apathy and preoccupation with drugs found in morphine maintenance. Approximately 82% of all patients can be considered successes. After 24 months 85% of those remaining in the program were in school or employed. Crime was reduced by 90% in the group.

The 15% scored as failures were patients with intractable alcoholism, abuse of nonnarcotic drugs, or psychopathic behavior. Previous studies of addicts under legal constraint recorded either failure or a moderate success over varying periods of time. A study of 269 methadone patients known to New York City and State probation or parole authorities shows a record of 72% retention in the program. Patients may need guidance in addition to the methadone. 19 references.

070247 Wyatt, Richard J.; Chase, Thomas N.; Scott, Jimmy; Snyder, Frederick; Engleman, Karl. National Institute of Mental Health, Bethesda, Maryland 20014 Effect of L-dopa on the sleep of man. *Nature.* 228(5275):999-1001, 1970.

In an investigation of the role of brain monoamines in the regulation of rapid eye movement (REM) and non-rapid eye movement (NREM) sleep in humans, the effect of L-dopa, the immediate precursor of dopamine and noradrenaline, was assessed. Placebo administrations and L-dopa treatment were given to 7 patients over a 2 week period at various dosages and studied by continuous all night recordings. L-dopa led to a reduction in the duration of REM sleep in all 7 patients. The decrease ranged from 4% to 46% of baseline. Moreover, the minutes from sleep onset to the first REM period (REM latency) increased from a mean of 47 min to 113 min. There was no change in the duration of NREM sleep. 16 references.

070267 Demaret, A. Departement de Psychologie Medicale et de Medecine Psychosomatique de l'Universite de Liege, Belgium /Comparison of the paroxysmal dyskinesias (neurodyslepsy) induced by the neuroleptics in man and the earliest behavior patterns of the new-born./ Comparaison entre les dyskinesies paroxystiques (neurodyslepsie) provoquees chez l'homme par les neuroleptiques et les premiers comportements du nouveau-ne. *Acta Psychiatrica Belgica (Brussels).* 70(4):562-578, 1970.

In order to discover to what normal behavior patterns the paroxysmal dyskinesias (neurodyslepsy) induced in man by the neuroleptics could correspond, neurodyslepsy was studied with respect to its biological, ontogenetic, and phylogenetic behavior. The dysfunctional appearance of the neurodysleptic syndrome was ignored. Fixed components in neurodysleptic behavior were recognized and their orientation studied. The following hypothesis was suggested: the neurodysleptic symptoms observed in men result from the elective pharmacological excitation of the neurophysiological structures that control the very earliest behavior patterns (inborn), both alimentary and visual; they are generally specific. The grasping behaviors, described by Spitz, are an example of these normal prototypes of neurodyslepsy. 11 references. (Author abstract modified)

070576 Blumberg, Arnold G.; Heaton, Audre M. Departments of Medicine and Biochemistry, Hillside Hospital, Glen Oaks, New York 11004 The occurrence of cyclohexylamine in urines studied for drug use by thin-layer chromatography. *Journal of Chromatography (Amsterdam).* 48:565-566, 1970.

The occurrence of cyclohexylamine in urines of psychiatric patients studied for drug use by thin layer chromatographic (TLC) procedures is reported. Extensive checks were made of a recurrent spot found on chromatograms from routine survey of urines for drugs. The conclusion has been reached that the spot represented cyclohexylamine, a breakdown product of cyclamate in the diet. It has also been concluded that cyclohexylamine may be confused with ephedrine or one of the amphetamines, and it is suggested that in the use of TLC procedures, cyclohexylamine standards be employed in interpreting findings. It was found that the incidence of appreciable excretion of cyclohexylamine in the urine of cyclamate users may be as high as 28% and as low as 7%, depending upon the population studied and the method of urine collection. There is an indication that psychiatric patients may have a higher incidence of cyclohexylamine excretion than the normal population. Conclusions may not be drawn from these results since our observations on psychiatric patients involved repeated urine collections and indeterminate dosages of cyclamates. Following cyclamate ingestion, the presence of cyclohexylamine in the urine, as determined by this method, may be variable. 7 references. (Author abstract modified)

070784 Feldman, Harold S.; Mulinos, Michael M. New Jersey College of Medicine and Dentistry, 24 Baldwin Avenue, Jersey City, New Jersey Nonaddictive psychotropic medication for imprisoned narcotic addicts. *Journal of the Medical Society of New Jersey.* 67(6):278-283, 1970.

Tybamate (2-methyl-2-propyl trimethylene butylcarbamate) is a tranquilizer chemically related

to meprobamate; therefore, it is potentially open to dependence and abuse. Direct attempts have failed to produce evidence of psychic or physical dependence on tybamate following prolonged administration of high doses to animals or humans. The present evaluation of tybamate was conducted with 24 male post-heroin addicts, inmates of a county penitentiary who had recently been detoxified. All subjects began on a divided daily dose of 3.5grams of tybamate which was increased each week. No withdrawal symptoms were observed on abrupt cessation of medication; there was no evidence of abnormal changes in liver or kidney function, hemoglobin concentration, formed elements of the blood, or composition of urine. Treatment with tybamate affected an appreciable rate of relief in symptoms of tension, anxiety, depression, emotional lability and other signs often experienced by former heroin addicts. The desire for heroin also decreased. Tybamate offers hope of satisfying some of the cravings of heroin addicts without addicting them to the substitute drug. 15 references.

070824 Van Woert, M. H.; Bowers, M. B., Jr. Departments of Internal Medicine, Pharmacology and Psychiatry, Yale University School of Medicine, New Haven, Connecticut The effect of L-dopa on monoamine metabolites in Parkinson's disease. ***Experientia (Basel).*** **26(2):161-163, 1970.**

The effect of L-Dopa on the abnormally low concentrations of homovanillic acid, 5-hydroxyindolacetic acid and tyrosine was measured in the cerebrospinal fluid and plasma of 14 patients with Parkinson's disease. After two months of L-Dopa therapy, at oral dosages of 4 to 7.5g/day the cerebrospinal fluid homovanillic acid concentration increased 18 fold. Plasma homovanillic acid concentration also increased the cerebrospinal fluid 5-hydroxyindolacetic acid concentration of Parkinsonian patients which decreased significantly during L-Dopa therapy. Plasma tyrosine decreased during L-Dopa therapy, but cerebrospinal fluid tyrosine did not change. 21 references.

070881 van Praag, H. M. Department of Biological Psychiatry, State University, Groningen, The Netherlands Indoleamines and the central nervous system: a sounding of their clinical significance. ***Psychiatria, neurologia, neurochirurgia (Amsterdam).*** **73(1):9-36, 1970.**

The synthesis and degradation of biogenic indolealkylamines were largely clarified and their cerebral function charted. Melatonin, a physiologically active 5-hydroxytryptamine derivative, was identified and proved to be selectively concentrated in the pineal gland. This refutes the view that this organ is a rudiment without function in higher mammals. It is probable that serotonergic 5-hydroxytryptamine mechanisms are involved in the regulation of temperature and sleep. Nitrogen methylation and oxygen methylation of indole alkylamines yield products with an hallucinogenic effect. The suspicion that the organism may be capable of such transformations is hardly a basis for a theory on the pathogenesis of schizophrenic psychosis. The 5-hydroxytryptamine hypothesis on the pathogenesis of certain types of depression is plausible. 186 references. (author abstract modified)

071705 Gantt, W. Horsley. The Pavlovian Laboratories, VA Hospital, Perry Point, Maryland Psychopharmacology and conditional reflexes. ***Conditional Reflex.*** **5(2):109-118, 1970.**

Drugs may be used in several ways to investigate their role in behavior. (1) Theplacebo effect is usually connected with the relation of the person to the drug. (2) Using the drug as an unconditional stimulus, its action may help to analyze the role of peripheral versus central stimuli in the formation of conditional reflexes; work has shown that the effect of drugs which act solely at the peripheral nerve endings without the involvement of the central nervous system cannot become conditioned. (3) The action of drugs on the conditional reflex (CR) compared with their action on the unconditional reflex (UR) explains some of their behavioral effects. (4) Schizokinesis is often prominent in the action of drugs. Although a drug may increase the level of the heart rate, for example, it can, on the other hand, diminish the reactivity shown in the CR. Meprobamate and mescaline affect differently the cardiacand the motor components of the CR, illustrating a schizokinesis. (5) The type of individual is an important factor in the action of drugs; the same drug may have opposite effects on different individuals. This leads to the conclusion that a drug should fit the individual as well as the disease. (6) Autokinesis is often seen in drug action. Therefore a single dose of some drugs, such as acetylcholine, epinephrine or LSD, may permanently change the relationships

between excitation and inhibition, in the direction of improvement or deterioration (positive or negative autokinesis). 22 references. (journal abstract modified)

071972 Paul, Michael I.; Ditzion, Bruce R.; Janowsky, David S. Laboratory of Chemical Pharmacology, National Heart and Lung Institute, National Institutes of Health, Bethesda, Maryland Affective illness and cyclic-A.M.P. excretion. ***Lancet (London).*** **No. 7637:88, 1970.**

The relationship between affective illness and cyclic A.M.P. urinary excretion is reported in a letter to the editor. Twenty four hour urinary excretions were studied in 37 patients with affective disorders at the National Institute of Mental Health and analyzed for cyclic adenosine 3',5'-monophosphate (cyclic A.M.P.). Manic patients had significantly greater 24 hour excretions of cyclic A.M.P. than did normal subjects, psychotic depressives, or psychoneurotic depressives. Excretion of cyclic A.M.P. was significantly higher in psychoneurotic depressives than in psychotic depressives. 2 references.

071987 Corey, Margaret J.; Andrews, J. C.; McLeod, M. Josephine; MacLean, J. Ross; Wilby, W. E. Department of Pediatrics, Room 2L-D1, Sir Charles Tupper Medical Building, Dalhousie University, Halifax, Nova Scotia, Canada Chromosome studies on patients (in vivo) and cells (in vitro) treated with lysergic acid diethylamide. ***New England Journal of Medicine.*** **282(17):939-943, 1970.**

Ten subjects with no record of prior use of d-lysergic acid diethylamide 25 (d-LSD 25) were given the drug. Blood samples were taken immediately before LSD therapy and 24 hours after treatment. Before treatment, the mean frequency of chromosomal breakage was 5.7. After the treatment, the frequency of chromosomal breakage was 4.9. Another study included patients who had dosages of LSD varying from 200 to 4350 micrograms over periods ranging from 24 hours to 8 years. The study included 4 groups: 5 patients treated with d-LSD only; 5 treated with mescaline sulfate only; 6 treated with both d-LSD 25 and mescaline sulfate; and 13 control subjects exposed to neither drug. The total number of breaks per 100 cells ranged from 6 to 12 for LSD, 2 to 13 for mescaline, 2 to 11 for both LSD and mescaline; and 2 to 17 in the control group. The results showed that within the LSD treated population, there was no relation between the frequency of aberrations and either LSD dosage or the time elapsed between treatment and sampling. In an in vitro study, the frequency of chromosomal breaks was increased in replicate cultures from each of 10 subjects when 1 microgram/ml of d-LSD 25 was added during the last 24 hours of culture. There appeared to be no cytogenetic evidence that d-LSD 25 given therapeutically produces chromosomal damage. 9 references.

071989 Forrest, Fred M.; Forrest, Irene S.; Serra, Mauricio T. Veterans Administration Hospital, Palo Alto, California Modification of chlorpromazine metabolism by some other drugs frequently administered to psychiatric patients. ***Biological Psychiatry.*** **2(1):53-58, 1970.**

Phenobarbital sodium and Aludrox, as representative of sedatives or antacids frequently prescribed for patients on chronic phenothiazine therapy, were studied with regard to their effect on urinary chlorpromazine excretion. Phenobarbital as an inducer of additional drug metabolizing enzymes in hepatic microsomes, was found to increase the rate of urinary chlorpromazine excretion by 10 to 18%. Conversely, epileptic patients normally receiving maintenance barbiturates in addition to chlorpromazine, showed 17 to 55% decreases in urinary chlorpromazine excretion when their barbiturates were withdrawn for 7 days. Phenobarbital sodium may be of interest in cases of acute chlorpromazine toxicity. Aludrox decreased the urinary chlorpromazine excretion rate by 10 to 45%, thus lowering chlorpromazine efficiency. 11 references. (author abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

069579 Manno, Joseph E.; Kiplinger, Glenn F.; Haine, Susan E.; Bennett, Ivan F.; Forney, Robert B. Indiana University Medical Center, Indianapolis, Indiana Comparative effects of smoking marihuana or placebo on human motor and mental performance. ***Clinical Pharmacology and Therapeutics.*** **11(6):808-815, 1970.**

The results of a comparative study using marihuana and placebo cigarettes to determine the effects on human motor and mental performance are reported. Motor and mental performance was tested after smoking a placebo cigarette and after smoking a marihuana cigarette calibrated to deliver 5mg. of delta-9-tetrahydrocannabinol. A

significant decrement in all motor performance tests and in 5 of 9 mental performance tests was observed after the marihuana cigarette. No cannabinols were detected in the blood or urine of subjects who smoked the marihuana. 15 references. (Author abstract modified)

070024 Rapoport, J. L.; Lott, I. T.; Alexander, D. F.; Abramson, A. U. National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland Urinary noradrenaline and playroom behaviour in hyperactive boys. ***Lancet.*** **2(7683):1141, 1970.**

The findings of an inverse relationship between urinary adrenaline and degree of hyperactive behavior and an inverse relationship between urinary noradrenaline and improvement in the symptoms of hyperactivity during dextroamphetamine administration provide some support for the hypothesis that a disturbance in noradrenaline metabolism may be associated with a subgroup of hyperactive children. 3 references.

070303 Guest, A. D. L.; Duncan, Catherine; Lawther, P. J. MRC Air Pollution Unit, St. Bartholomew's Hospital Medical College, London, England Carbon monoxide and phenobarbitone: a comparison of effects on auditory flutter fusion threshold and critical flicker fusion threshold. ***Ergonomics (London).*** **13(5):587-594, 1970.**

In a small series of experiments, 8 healthy subjects breathed either air alone or a mixture of air and carbon monoxide designed to raise carboxyhemoglobin saturations to approximately 10%. Neither Ss nor operators knew which gas was administered, and the effects of the exposures on auditory flutter fusion thresholds and critical flicker fusion thresholds was assessed during a period of 6 hours after the end of the exposure. There was no evidence of any depressant effect of carbon monoxide on the thresholds: the auditory flutter fusion threshold increased a little with carbon monoxide. To check the response of the Ss to a drug that had already been tested, the experiments were repeated, with oral administration of phenobarbitone and a placebo. For the group as a whole there was a depressant effect of phenobarbitone on both of the thresholds, as expected. 12 references. (Author abstract)

070352 Friedman, Philip H.; Buck, Ross; Allen, Vernon L. Department of Behavioral Science, Temple University Medical School, Philadelphia, Pennsylvania Arousal, anxiety, aggression, and attitude change. ***Journal of Social Psychology.*** **82:99-108, 1970.**

The effects of an aggressive habit and emotional arousal, measured by heart rate, blood pressure, and self-report, on 2 types of attitude change were investigated. The Ss were injected with epinephrine or placebo, and acquired an aggressive or nonaggressive habit. Then Ss read an article attacking teaching machines and were told that the injected 'vitamin' would relax them. Results showed that psychological arousal was positively related to degree of influence by the relaxation communication, but physiological arousal and an aggressive habit were not. Aggressive habit Ss and to a lesser extent physiologically aroused Ss were most influenced by the teaching machine article. 12 references. (Author abstract)

070778 Husemann, F.; Kugler, J.; Frank, I. Neuroclinic of the University, 7 Nussbaumstrasse, 8 Munich 15, Germany Relaxing effect of vitamin-B with anabolics. Entspannungsfordernde Wirkung von Vitamin B mit Anabolica. ***Arzneimittel-Forschung (Aulendorf).*** **20(4):557-560, 1970.**

A 12 day study was performed on 3 male and 3 female patients with various neurologic disorders using Megagrisevit and placebo alternately in 3 day periods. In half of the patients EEG studies showed pronounced changes after 3 days of treatment with the drug compared to placebo. The curves could be interpreted as a slight decrease of attention accompanied by decrease of psychic tension and transitory, reversible periods of sleepiness. Cardioinhibitory, vasodepressor side-effects or changes of the average visual responses were not observed. Megagrisevit can be used in combined therapy of certain psychotic disorders when general condition and metabolism render therapy with Vitamin-B and anabolic steroids desirable in the patient. 9 references. (author abstract modified)

070933 Hort, V.; Vojtechovsky, M.; Brezinova, V.; Soukupova, B.; Safratova, V. Psychiatric Clinic, Ke Karlovu 11, Prague 2, Czechoslovakia Modification of the scopolamine effect by sleep deprivation. ***Activitas Nervosa Superior (Praha).*** **12(1):53-54, 1970.**

The interaction of scopolamine with sleep deprivation was studied in a group of nonpsychotic alcoholics. Clinical analysis revealed that sleep deprivation affected the scopolamine

influence on mnestic functions and that the dominant syndrome of scopolamine interaction with sleep deprivation was confusion. The relationships between sleep and the cholinergic mechanisms participating in vigilance and memory is discussed. 6 references.

070934 Brezinova, V.; Hort, V.; Vojtechovsky, M. Psychiatric Clinic, Ke Karlovu 11, Prague 2, Czechoslovakia The effect of centrophenoxine on EEG vigilance in the course of sleep deprivation and on the EEG pattern of all-night sleep. *Activitas Nervosa Superior (Praha).* 12(1):54-56, 1970.

The effect of centrophenoxine on EEG vigilance in the course of sleep deprivation and on the EEG pattern of all night sleep, was studied in 2 experiments. In the first experiments, 12 abstinent chronic alcoholics were deprived of sleep for 127 hours. Six subjects received lg of centrophenoxine during deprivation; 6 subjects received no medication. In the second experiment, all night sleep was studied before, during and after the administration 750mg of centrophenoxine per day. Centrophenoxine had a favorable effect on lower vigilance level during the course of sleep deprivation; it reduced the amount of the deepest slow wave sleep stages and maintained EEG arousal reaction to stimuli for a longer time. With regards to all night sleep,centrophenoxine prolonged the time of falling asleep, reduced the amount of the deepest synchronous sleep stages (3 and 4) and did not reduce the amount of phase 1 REM sleep significantly. 4 references.

070955 Soukupova, B.; Vojtechovsky, M.; Safratova, V. U Ctvrte Baterie 194, Prague 6, Czechoslovakia Drugs influencing the cholinergic system and the process of learning and memory in man. *Activitas Nervosa Superior (Praha).* 12(1):91-93, 1970.

The dependence of memory processes on central cholinergicmechanisms was studied in experiments on 12 healthy students. The effects of 3 basic anticholinergics, scopolamine, atropine and benactyzine on mnestic functions were evaluated. The process of learning paired associations was significantly facilitated by physostigmine, contrary to dexfenmetrazine, which produced only a slight effect. The observed results confirm the original hypothesis of the relationship of cholinergic mechanisms to a deterioration of recent memory in chronic alcoholics. 4 references.

070968 Pollack, Max. Department of Psychology, Queens College of the City University of New York, Flushing, New York Chlorpromazine and CNS changes in man. *In: Smith, W., Drugs and cerebral function.* Springfield, Illinois, Charles C Thomas, 1970. 288 p. (p. 41-53).

The roles of chlorpromazine (CPZ) and electroconvulsive therapy (ECT) in psychiatric patients are discussed from a neurophysiological and psychological viewpoint. Scores on 17 psychological tests and 5 EEG variables were investigated in CPZ treated (1200mg) patients, and in ECT treated patients, all suffering from schizophrenia, psychotic depressions or character disorders and psychoneurosis. CPZ significantly affected performance in 9 of the 17 tests with all except the Rorschach test showing impairment. Overall multivariate association was also found between CPZ induced EEG changes and psychological test performance. Treatment of a separate but similar group of patients with grand mal convulsive treatments (3 times weekly) revealed pronounced EEG slow wave activity increases and an abnormal EEG pattern. Memory loss and disorientation were also noticed. All psychological tests except the rod and frame, delayed auditory feedback and two hand coordination tests showed significant impairment. The induced changes in psychological test scores are similar to changes found in studies of aged persons. It is suggested that the efficacy of CPZ for treatment of schizophrenia may be associated with the drug's effect on the sleep waking patterns of patients. 29 references.

070972 Turner, William J. Consultant, Dreyfus Medical Foundation, New York, New York Dilantin effect on emotionally disturbed children. *In: Smith, W., Drugs and cerebral function.* Springfield, Illinois, Charles C Thomas, 1970. 288 p. (p. 99-102).

The beneficial effects of diphenylhydantoin (DPH) on children with emotional and behavioral problems of a nonepileptic nature are discussed. Results are presented on the Block Design Test in 9 patients, all but two of whom showed improvement. Dosages from 100 to200mg daily were given to the children, aged 6 to 13 years. All but two children showed marked improvement in the raw score on the Block Design Test and the subjects generally showed behavioral normalization after 1 month of DPH therapy. School problems, temper tantrums, restlessness and overactivity were the most common pretreatment symptoms. 4 references.

070973 Haward, Lionel R. C. Biometric Clinic, Chichester, Sussex, England Effects of sodium diphenylhydantoinate and pemoline upon concentration: a comparative study. *In: Smith, W., Drugs and cerebral function.* Springfield, Illinois, Charles C Thomas, 1970. 288 p. (p. 103-120).

A comparison is made between the effects of sodium diphenylhydantoinate (DPH) and pemoline on concentration. A simulated air traffic control situation was used to assess the ability of pemoline to combat fatigue. Twenty males (30 years or older) were trained on the simulator system and several runs were taken before and after administration of a 20mg dose. This optimum dose, administered in a double blind manner, caused a significant decrease in errors, although later studies with 40 and 60mg doses showed impairment in functioning. In another test twelve college students (19 to 21 years) were selected for the air traffic control task and after two trials of 2 hour duration received 150mg of phenytoin or a placebo. In this test the target symptom was the concentration impairing condition anancastia, in which concentration is impaired by preoccupation with irrelevant topics of thought. Significant improvement was noted with phenytoin, although it showed none of the side effects characteristic of stimulants. It is theorized that pemoline acts to counter the physical components of mental fatigue while DPH acts on the psychological components producing efficient use of physical potential. 85 references.

071336 Eisdorfer, Carl; Nowlin, John; Wilkie, Frances. Center for the Study of Aging and Human Development, Duke University Medical Center, Durham, N. C. 27706 Improvement of learning in the aged by modification of autonomic nervous system activity. *Science.* 170(2964):1327-1329, 1970.

A study was conducted to determine whether learning in older persons can be improved by drugs and whether a state of heightened rather than depressed end organ arousal is responsible for decrement in learning in the aged. Partial blockade of beta adrenergic end organ response to the autonomic nervous system was effected in a group of older men by administration of propranolol. The result was improved performance in a learning task. The data support the hypothesis that the learning decrement found among older men is not simply a manifestation of structural change in the central nervous system but is, at least in part, associated with the heightened arousal of the autonomic nervous system that accompanies the learning task. 16 references. (Author abstract modified)

071998 Melges, Frederick T.; Tinklenberg, Jared R.; Hollister, Leo E.; Gillespie, Hamp K. Department of Psychiatry, Stanford University School of Medicine, Stanford, California Marihuana and temporal disintegration. *Science.* 168(3935):1118-1120, 1970.

Temporal disintegration means that the individual has difficulty in retaining, coordinating and serially indexing those memories, perceptions and expectations that are relevant to the goal he is pursuing. High oral doses of tetrahydrocannabinol induce temporal disintegration in normal subjects. This phenomenon stems partly from impaired immediate memory. Temporal disintegration is associated with disorganized speech and thinking. Temporal disintegration was measured by a task, termed the goal directed serial alternation, which required that the subject simultaneously hold in mind and coordinate information as well as mental operations relevant to pursuing a goal. One cognitive task which was relevant to short and long-term memory was the regular serial subtraction of sevens. With increasing doses of tetrahydrocannabinol extracted from marihuana there were no significant mistakes in long-term memory. Short-term memory, however, was impaired. 7 references.

072032 Cassell, W. A.; Hemingway, P. Psychiatric Services Branch, Provincial Health Building, Regina, Saskatchewan, Canada Body consciousness in states of pharmacological depression and arousal. *Neuropharmacology (Oxford).* 9(2):169-173, 1970.

Body consciousness in states of pharmacological depression and arousal were studied using Fisher's Body Focus Questionnaire. Altered levels of CNS excitation were produced by phenobarbital and caffeine citrate. Under the former conditions, it was observed that the more sedated an individual felt, the more his body consciousness focused on the head. Fisher's 'high barrier' subjects were found to be particularly sensitive to the depressant drug. With stimulation, a positive relationship was found between the degree of arousal and the extent a subject focused on outer and right aspects of the body. This was more prominent in the 'low barrier group'. 21 references. (author abstract modified)

072147 Kurland, Albert A.; Pinto, Alcides; Destounis, Nicholas; Babikow, Paul W. Maryland Psychiatric Research Center, Baltimore, Maryland 21228 Effects of trimeprimine (Surmontil) on spermatogenesis and mood in normal volunteers. *Current Therapeutic Research.* 12(4):186-191, 1970.

The effects of trimeprimine on mood and spermatogenesis were studied over an 8 week period in 11 normal volunteers. Significant weight gains were observed. Intellectual functioning was not significantly affected, as indicated by objective psychological testing, but some changes in mood were reported on a self rating scale. A transient rise in transaminase was noted. Other side-effects were minimal. Posttreatment seminal analysis showed decrease of sperm count, volume and motility, but these changes were within the normal range. 14 references. (author abstract)

072155 Faroux, C.; Furon, D. Service de Reanimation respiratoire, Hopital Albert-Calmette, 59-Lille, France /Clinical study of a psychotropic drug: sulpiride in attempted suicide without psychosis./ Etude clinique d'un psychotrope: le sulpiride dans une population de suicidants non psychotiques. *Semaine des Hopitaux de Paris (Paris).* 46(29B):104-108, 1970.

Suicidal tendencies were studied on an intensive care unit in a mixed population of 93 subjects including 60 women and 33 men. Suicide attempts were most frequent between the ages of 17 and 25 years, but a second peak was noted at about the age of 60. The attempt, occurring during reactionary depression, often revealed neurotic personalities who were until then well compensated, and often attracted attention to cases difficult to classify: e.g. prepsychotic subjects, psychopathic disturbance, character neurosis, emotional instability, psychosomatic conversion. The affective problems and lack of professional adaptation often seemed to be the precipitating cause. Suicide was attempted mainly by ingestion of hypnotics, sedatives or analgesics. Once the poison had been eliminated, 68 patients were given sulpiride alone, and 25 a combination of sulpiride and diazepam. The stimulant effect on mood and vigilance, speech facilitation and improved contact isemphasized. The ease of presciption and improved praxis were important factors in dialogue and professional - patient relations. (author abstract)

072216 Evans, J. I.; Ogunremi, O. Department of Psychiatry, Edinburgh University, Edinburgh EH10 5HF, Scotland Sleep and hypnotics: further experiments. *British Medical Journal (London).* No. 5718:310-313, 1970.

Two experiments compatible with that used to investigate the effect of clinical doses (200mg) of amylobarbitone were set up to investigate the effects of clinical doses of chloral hydrate (800 mg), dichloral phenazone (1,300mg), and Mandrax (methaqualone 250mg and diphenhydramine 25mg) over a period of 1 to 2 weeks. Four healthy male subjects were used in each experiment and received placebo or drug throughout a period of 6 to 8 weeks when control records, drug records, and drug withdrawal records were obtained. Chloral hydrate was found to depress rapid eye movement (R.E.M.)sleep appreciably though less consistently than amylobarbitone. No withdrawal R.E.M. sleep rebound was found. Neither dichloralphenazone nor Mandrax was found consistent to depress R.E.M. sleep, though occasional nights when R.E.M. sleep was low occurred more often with Mandrax. In the light of other experiments it is postulated that there exists a 'threshold' in the dose of a hypnotic, and that when this is exceeded the drug will produce R.E.M. reduction. Thus it may be possible to prescribe a drug which is clinically useful while avoiding withdrawal effects. 21 references (author abstract)

15 TOXICOLOGY AND SIDE EFFECTS

069580 Vacaflor, L.; Lehmann, H. E.; Ban, T. A. Douglas Hospital, 6875 LaSalle Blvd., Verdun, Quebec, Canada Side effects and teratogenicity of lithium carbonate treatment. *Journal of Clinical Pharmacology.* 10(6):387-389, 1970.

Adverse reactions and teratogenicity of patients to lithium carbonate treatment are reported as part of a study to test the therapeutic and prophylactic effects of its administration. In a course of a clinical trial with lithium carbonate in patients suffering from periodic affective disorders, numerous side effects occurred.Among these, tremor and diarrhea were most frequent. Generalized maculopapular rash and alopecia were seen in 1 patient each, and a toxic confusional state, in 4. One patient delivered a malformed baby while on lithium carbonate and chlorpromazine treatment. In the same patient, restriction of salt intake, administration of a diu-

retic, and suspected unauthorized overdosage of lithium intake induced a severe but reversible comatose state with generalized and focal convulsions. 3 references. (Author abstract modified)

069613 Bialos, Donald S. Department of University Health, Division of Student Mental Hygiene, Yale University, 1505-A Yale Station, New Haven, Connecticut 06520 Adverse marijuana reactions: a critical examination of the literature with selected case material. ***American Journal of Psychiatry.*** **127(6):819-823, 1970.**

After reviewing the literature it is concluded that there is a tendency to designate as adverse any reactions to marijuana that are psychotomimetic or anxiety provoking or that interfere with functioning. It is felt that the definitions of the term 'adverse marijuana reactions' are ambiguous. Before the term is applied, the user's character structure, expectations of the experience, environmental factors present at the time of ingestion, and the amount ingested should be taken into account. 14 references. (Journal abstract)

070412 Guttman, H.; Lehmann, H. E.; Ban, T. A. Douglas Hospital, 6875 LaSalle Blvd., Verdun, Quebec, Canada A survey of extrapyramidal manifestations in patients attending an after care clinic of a psychiatric hospital. ***Laval Medical.*** **41(4):449-455, 1970.**

The incidence of drug induced extrapyramidal signs in relation to age, sex, diagnosis, hospitalization and treatment was studied in the 454 of the After Care Clinic population of the Douglas Hospital. The following findings were obtained: 1) Twenty one percent of the population studied presented extrapyramidal signs; 2) More specifically, 14% of the total clinic population studied presented the bucco oral syndrome; 3) Bucco oral dyskinesia was found to be more common among females, while akathisia was more prevalent among males; 4) The median age of patients with extrapyramidal signs, especially of males, was more than that of the clinic population as a whole and of those with bucco oral syndrome greater than that of all patients with extrapyramidal signs; 5) Older patients receiving high dosages of neuroleptics developed extrapyramidal signs more frequently than younger patients; 6) Drug dosage as a cumulative factor was most consistently related to the production of extrapyramidal signs including the bucco oral syndrome; 7) When equal cumulative doses are given the time factor becomes important in that large doses of phenothiazines given during a short period of time are more likely to produce extrapyramidal signs than lower doses over a longer period. 1 reference. (Author abstract)

070854 Coull, D. C.; Crooks, J.; Dingwall-Fordyce, I.; Scott, A. M.; Weir, R. D. Department of Pharmacology and Therapeutics, The University, Dundee DD1 4HN, Scotland Amitriptyline and cardiac disease: risk of sudden death identified by monitoring system. ***Lancet (London).*** **2(7673):590-591, 1970.**

A hospital based drug information system has been used to investigate a suspicion linking unexpected death with the administration of the tricyclic antidepressant, amitriptyline, in patients with a diagnosis of cardiac disease. Six out of 53 patients with cardiac disease who were identified by the system died suddenly and unexpectedly after administration of the drug, compared with none of 53 control patients matched for sex, age, diagnosis, and length of stay in hospital. This high frequency of unexpected death was not found in patients receiving imipramine, nor in patients without cardiac disease receiving amitriptyline. Patients on amitriptyline showed a lower incidence of myocardial infarction, cardiac failure, and significant anemia. Nevertheless, in view of the mortality among amitriptyline treated patients, amitriptyline should be used with caution in patients with cardiac disease. 5 references. (author abstract modified)

070899 Zupko, Arthur G. Brooklyn College of Pharmacy, Long Island University, Brooklyn, New York A practical guide to drug interactions. ***Resident and Staff Physician.*** **16(3):52-64, 67-69, 73, 1970.**

The guide is a compendium of known drug interactions arranged in 15 therapeutic categories. Interactions are covered from the viewpoint of pH and chemical interaction, neuronal and hormonal effects, enzymatic potentiation or inhibition, and bacterial effects (i.e. bacteriostatic vs. bacteriosidal action). The categories covered are: acidifiers, alkalizers, analgesics, antibiotics, anticoagulants, antidepressants, antidiabetics, antihypertensives, barbiturates, diuretics, hormones, muscle relaxants, uricosuric agents, and a catchall of miscellaneous drug interactions.

070945 Sedivec, V.; Valenova, Z.; Paceltova, L. Dukelska 69, Plzen, Czechoslovakia Persistent extrapyramidal oral dyskinesias following treatment withthymoleptics. ***Activitas Nervosa Superior (Praha).*** **12(1):67-68, 1970.**

Persistent extrapyramidal oral dyskinesis was observed in patients during treatment with phenothiazines and similar drugs. These side -effects of therapy with thymoleptics were manifested as involuntary movements of circumoral muscles, lips and tongue. Antiparkinsonian drugs failed to influence oral dyskinesias; withdrawal of the thymoleptics was without effect. 2 references.

070957 Guensberger, E.; Tesarova, O. Psychiatricka Klinika Bratislava, Mickiewiczova 13, Czechoslovakia /Psychopathological side-effects of sedatives./ Sprievodne psychopatologicke javy sedacie. ***Activitas Nervosa Superior (Praha).*** **12(1):95-96, 1970.**

The pathological side-effects of sedatives were studied in psychotic and neurotic patients. Three groups could be distinguished according to the side-effects. In group 1, an attenuation of pathological symptoms was observed in 21 psychotic and 24 neurotic patients. The most frequent symptoms observed were: autism, abulia, apathy, emotional changes, memory disturbances, and accentuation of paranoia. In group 2, depression, the Misch syndrome and apathy were observed in 52 psychotics and 14 neurotics. The last group of patients was characterized by neurotic syndromes and emotional lability. The therapeutic value of sedatives in different psychotic disorders is discussed.

071241 Kalensky, J.; Herzka, H. S. Psychiatrische Poliklinik fur Kinder und Jugendliche, Zurich, CH-8028 Zurich, Switzerland /Epilepsy therapy with mentally retarded children: neuropsychiatric disorders through diphenylhydantoin./ Zur Epilepsietherapie bei geistig behinderten Kindern: Neuropsychiatrische Storungen durch Diphenylhydantoin. ***Therapeutische Umschau (Bern).*** **27(7):457-459, 1970.**

Problems of diagnosing diphenylhydantoin intoxication in epileptic children with serious mental deficiencies and physical handicaps are discussed, based on a 1 year study of 8 epileptic children confined in a home for theseverely mentally retarded. Neuropsychiatric symptoms of diphenylhydantoin intoxication in children (ataxia, nystagmus, apathy, mydriasis, muscle hypotonia with hyporeflexia, loss of appetite, numbness) are not as pronounced as they are in adults; symptoms in children disappear more rapidly, which makes diagnosis of drug intoxication much more difficult. For instance, the underlying symptoms of brain damage can be disguised by neuropsychiatric symptoms brought on by diphenylhydantoin intoxication. Behavioral problems are often preexisting conditions. The weight and age of the patient are critical factors to consider in administering the drug, especially in mentally retarded children. 10 references.

071258 Reimold, W. V.; Larbig, D.; Kochsiek, K. Medizinische Klinik und Poliklinik der Universitat, 34 Gottingen, Humboldtallee 1, Germany /Hypokalaemia and arrhythmias as a result of quinine poisoning./ Hypokaliamie und Herzrhythmusstorungen infolge Chininvergiftung. ***Deutsche Medizinische Wochenschrift (Stuttgart).*** **95(10):517-521, 1970.**

A case study of the effects of quinine hydrochloride poisoning is presented. A 20 year old girl swallowed 12.5g of quinine hydrochloride in an attempt to induce abortion. Within 30 minutes there were acute symptoms of poisoning: pressure in the head, fogged vision, disturbances of equilibrium, and irregular heart beats, followed by partial hearing loss, vomiting and, after 7 hours, green blindness, tachycardia and extrasystoles from several foci (in the ECG). The ventricular extrasystoles at times gave rise to quadrigeminal rhythm, at times to chaotic heart action, so that the onset of ventricular fibrillation had to be feared. An important cause of the arrhythmia was probably hypokalemia (K + 2.6mEq/1, 15 days after the drug had been taken). Administration of potassium (20mEq KC1, in the first hour) rapidly stopped the ventricular extrasystoles. In the acute stage of poisoning, hypokalemia and arrhythmias are lekely to occur in every case; ajmalin and related drugs are contraindicted for quinine intoxication. Sodium lactate and sodium bicarbonate should not be given for hypokalemia without simultaneous potassium substitution. Forced diuresis and, in severe cases, peritoneal dialyses are essential for rapid elinination of the drug. In the case described, the hypokalemia and nodal extrasystoles persisted even after the acute toxic stage, requiring potassium administration for several months. An arrhythmia was still present after 12 months (nodal

extrasystoles). 25 references. (journal abstract modified)

071929 No author. Author address not given Narcotic analgesics -- II. Adverse effects. *British Medical Journal (London).* No. 5709:587-588, 1970.

Adverse effects of various analgesics are described. Itgenerally takes about 1 to 2 weeks with therapeutic doses of morphine given several times daily to produce mild symptoms of withdrawal when the morphine is discontinued. Dependence on one drug usually means that substituting another produces little difference in effect (cross-dependence), though replacing morphine with pethidine may not be satisfactory, since pethidine does not have the same sedative action and withdrawal symptoms may occur. Withdrawal of morphine symptomstypically seen include: lacrimation, yawning, perspiration, restless sleep, hallucinations, irritability, dilated pupils, anorexia, nausea, vomiting and diarrhea. These effects are far less after amidone, but more intense and shorter lasting after pethidine. Other effects of narcotic analgesics include: respiratory depression, emetic sequelae (with morphine 40 percent of patients are nauseated and 16 percent vomit), meiosis, dizziness, mental clouding, constipation, biliary and renal tract spasm, allergic phenomena and increased sensitivity to narcotic analgesics (after third decade). Narcotics and monoamine oxidase inhibitors used together may cause fatal hypotension or coma. Other cortical depressants such as tranquilizers, do summate with narcotics, so that when used together the dose of analgesic should be reduced. The immediate treatment of acute life threatening respiratory depression is artificial respiration. Nalorphine (5mg increments i.v. or i.m.,at 15 min intervals) and levallorphan (1mg i.v. followed by 0.5mg increments) both reverse the respiratory depressant effects of narcotic drugs. 20 references.

071949 Meadow, S. R. Department of Pediatrics, Guy's Hospital, London, England Congenital abnormalities and anticonvulsant drugs. *Proceedings of the Royal Society of Medicine (London).* 63(1):48-49, 1970.

The hypothesis is put forward that the apparent increased incidence of babies with cleft lip and/or palate born to epileptic mothers is due to factors other than chance. Of 32 such cases reported born to epileptic mothers receiving anticonvulsant therapy (phenobarbitone, phenytoin, primidone, troxidone), 11 had other major congenital abnormalities involving the cardiovascular and skeletal systems. It is recommended that a study should be undertaken to determine: (1) if there is an increased incidence of cleft lip and/or palate in babies born to epileptic mothers, and (2) if it is linked with the maternal disease or the anticonvulsant drugs. Genetic factors should be considered as well as the role of the anticonvulsants as folic acid antagonists. 6 references.

071960 Healy, Joan M.; Van Houten, Patricia L. Queens Children's Hospital, Bellerose, New York 11426 Effect of psychotomimetic agents on sex ratio? *Lancet (London).* No. 7672:574, 1970.

In a letter to the editor, a study reported by Aase in a previous issue is discussed. It is noted that the offspring of 10 women who had taken LSD during pregnancy were all female; the probability of the offspring of any 10 pregnancies all resulting in children of the same sex is 1 in 1024. It has been reported that women who became schizophrenic within a month of conception likewise gave birth to female infants only. There is reason to believe that there exists a common etiological basis for the changes of secondary sex ratio which follow LSD ingestion and those after the onset of schizophrenia during the first month of pregnancy. Thus, the hypothesis that the same factors leading to a psychotomimetic reaction in normal people also lead to the psychosis features of schizophrenia requires reevaluation in the light of this recent data. 5 references.

071968 Bleiweiss, Herman. Instituto de Genetica Medica, Sarmiento 2569, Buenos Aires, Argentina Salt supplements with lithium. *Lancet (London).* No. 7643:416, 1970.

In a letter to the editor, it is recommended that extra sodium chloride be administered to eliminate the side-effects of lithium carbonate. Nine patients, 8 of whom had manic-depressive psychosis, manic state, were given an initial dose of lithium carbonate of 600mg 3 times daily. The dose was gradually increased to 2.7g daily together with 0.5to 1.0g of sodium chloride 3 times daily. The only side-effect noted was a fine hand tremor in one patient which later disappeared.

071970 Edgell, P. G.; Peterfy, G.; Pinter, E. J. Department of Psychiatry, Reddy Memorial Hospital, Montreal, Canada Lithium toxicity. *Lancet (London).* No. 7643:415-416, 1970.

In a letter to the editor, it is reported that 1 out of 4 patients randomly selected for lithium treatment showed a toxic reaction necessitating intensive supportive care. Three patients responded favorably to 300mg twice or 3 times daily. The fourth patient, a 68 year old woman suffering from involutional melancholia and primary hypothyroidism, exhibited slurred speech, unsteady and ataxic gait, and a deteriorating level of consciousness after 24 days of lithium carbonate treatment (300mg 3 times daily). Her skin was flushed and there were signs of dehydration. Thus, caution is necessary intreating patients with metabolic or endocrine disorders when lithium is being given. 1 reference.e

071971 Hessov, Ib. Department of Psychiatry, Slagelse Central Hospital, Denmark Hypertension during imipramine treatment. ***Lancet (London).*** **No. 7637:84-85, 1970.**

A case history is reported in a letter to the editor of a 57 year old woman admitted to the hospital with endogenous depression, who developed hypertension as a result of treatment with imipramine. Two blood pressure measurements of 140/90 mm Hg and 140/85 mm Hg were taken before treatment. After 9 days on a daily dose of 150mg imipramine, the blood pressure was 175/120 mm Hg. Reduction of the dose of imipramine to 100mg daily did not lead to a fall in blood pressure, so the drug was withdrawn. When the blood pressure was at its highest, the 24 hour excretion of noradrenalin, adrenalin and vanilmandelic acid was within normal range. 6 references.

072149 Baker, A. A. Department of Health and Social Security, London, S.E. 1, England Hospital admissions due to lysergic acid diethylamide. ***Lancet (London).*** **No. 7649:714-715, 1970.**

Case reports of 67 patients admitted to a hospital for drug addiction during 1966 and 1967 were studied to assess the role of lysergic acid diethylamide (LSD) in the admission. Direct involvement of LSD was implicated in 26 cases with acute psychotic reactions, 2 cases of attempted suicide, and 3 cases of aggressive outbursts, while partial involvement was evident in 26 cases where many different drugs had been used. In 10 cases no connection could be made between LSD and admission to the hospital. Examples of each type of situation are presented. 1 reference.

072156 Mouren, P.; Mayet, J.; Larrieu, A. Service des Maladies Nerveuses, Hopital Sainte-Marguerite, 13-Marseille, France /Clinical trial of a new molecule 'sulpiride' in psychiatric practice./ Essai clinique d'une molecule nouvelle, le sulpiride, en pratique psychiatrique. ***Semaine des Hopitaux de Paris (Paris).*** **46(29B):97-103, 1970.**

Choosing a wide range of indications among patients under treatment in hospital and in private practice, an attempt was made to analyze the properties of sulpiride, detect side-effects and determine the best mode of administration and duration of treatment. A careful search for side-effects brought to light a few states of excitation or aggressivity, rare neurologic manifestations such as tacykinesia, masseter muscle contractions, facial dyskinesia and tremor, a few endocrine disorders and an unusual skin rash. It is possible to associate the drug with all neuroleptic and thymoanaleptic drugs. The drug is original in its rapid action on mental automatism, mood and vigilance and in raising psychomotor inhibition. 24 references. (author abstract modified)

072406 Villeneuve, A.; Gagnon, A.; Deschambault, M. Division of Recherches, Hopital St-Michel-Archange, Quebec 5, Quebec, Canada /The effects of withholding of neuroleptics from mental patients./ Les effets du sevrage des neuroleptiques chez les malades psychiatriques. ***Laval Medical (Quebec).*** **41(4):512-521, 1970.**

In view of the eventual occurrence of irreversible side-effects, especially neurological ones, resulting from prolonged administration of neuroleptics, the possibility of alternating drug treatment with drug free periods is considered important. The withdrawal syndrome as well as its nature upon the discontinuation of medication was evaluated. Parameters concerning the autonomic nervous system, the cardiovascular system, the extrapyramidal system, and the blood chemistry andpsychiatric condition are discussed. These factors were studied in chronic female patients for 6 weeks after sudden withdrawal of neuroleptics. 24 references. (author abstract modified)

16 METHODS DEVELOPMENT

071747 Cameron, D. C. Division of Pharmacology and Toxicology, World Health Organization, Geneva, Switzerland Drug dependence: some research issues. ***Bulletin of the World Health Organization (Geneva).*** **43(4):589-589, 1970.**

A study examines some problems of drug dependence, stressing the importance of a balanced approach. Consideration must be given to the demand for, as well as the supply of, drugs. Without a demand, there would be no continuing supply of manmade agents and no need to control the availability of naturally occurring agents. To achieve a balanced approach, increased research is needed into the effects on man of taking various dependence producing drugs (particularly when these are used for long periods of time), the natural history of drug taking, the relative effectiveness of various preventive, therapeutic and restorative approaches and techniques, and means of identifying substances that, because of their dependence producing properties, are apt to induce individual or public health problems. Attention is also called to some problems that may inhibit, but do not preclude, the initiation of studies in the field of drug dependence. 16 references. (journal abstract)

072154 Martin, A.; Masson, J. M.; Thouvenot, J. Service de Psychiatrie des Femmes du C.H.R. Bretonneau, Boulevard Tonnelle, 37-Tours, France /Electrosplanchnography in anorexia nervosa and depression -- preliminary results./ L'electrosplanchnographie dans les anorexies mentales et les depressions -- premiers resultats. *Semaine des hopitaux de Paris (Paris).* 46(29B):54-60, 1970.

Electrosplanchnography (ESG) was conceived to evaluate overall digestive motor activity while avoiding disagreeable explorations. It is based on the recording of variations in abdominal skin potentials. This technique permits one to obtain a precise diagnosis and also to control the effects of treatment. It was mainly used to evaluate the effects of 2 substances, 1 with digestive effects, metoclopramide, the other a major neuroleptic drug, sulpiride. A first group of 44 patients was treated with metoclopramide, a second group of 79 patients was treated with sulpiride. The results confirm the central action of the 2 drugs, as shown by regulation of motor activity and reappearance of the gastro - colic reflex, especially in cases of anorexia nervosa. The action of sulpiride is here comparable with certain anxiolytics and disinhibitors but is much more intense. The ESG seems to demonstrate that various mechanisms (inhibition of cortical origin in anorexia nervosa, all round hypomotility in depressive psychoses) may be the cause of the refusal of food. 34 references. (author abstract modified)

070284 Newbold, H. L. Doctors Building, Asheville, North Carolina How one psychiatrist began using niacin. *Schizophrenia.* 2(4):150-160, 1970.

A psychiatrist reports both successes and failures in treating schizophrenic patients with niacin. It is concluded that niacin is a useful medication for many persons with schizophrenia. Personal reactions to niacin therapy are also reported. 12 references.

070830 No author. Author address not given Meprobamate loses some label claims. *Medical World News.* 11(41):5, 1970.

Drug review panels of the Federal Drug Administration (FDA) havejudged that meprobamate (Miltown, Wallace and Equanil, Wyeth) is ineffective as a skeletal muscle relaxant. The FDA has ordered its labeling changed to reflect this finding. Meprobamate is effective in relieving anxiety and tension and in promoting sleep in anxious, tense patients; however its effectiveness is uncertain against anxiety states associated with tension headache, medical and surgical disorders, heart disease and behavior disorders. The manufacturers of meprobamate have been given 6 months to prove that it is effective in treating chronic alcoholism and psychosis.

070897 Lennard, Henry L.; Epstein, Leon J.; Bernstein, Arnold; Ransom, Donald C. Author address not given Hazards implicit in prescribing psychoactive drugs. *Science.* 169(3944)438-441, 1970.

The increased regulation of personal and interpersonal processes by drugs, the implications attached and its long term effects were studied. The descriptions of the effects of psychoactive drugs provided in advertisements and circulars to physicians serve to perpetuate the use of drugs to alter states of consciousness and regulate behavior. Such advertising also implies that psychoactive drugs have a specificitry of effect which has not been demonstrated. A more appropriate model of drug action would be that, when any drug is introduced into an individual, it produces a range of systemic alterations in the psysiological system of the organism, some of which are desirable effect (main effect) and others of which may be undesirable effects (side-effect). There are 2 major kinds of costs that must be paid for the mystification surrounding psychoactive drugs: costs involving the individual, and his personal functioning and experience, and cost involving human rela-

tions in significant social systems within which the drugged person lives. 11 references.

070924 Vinar, O. Vyzkumny Ustav Psychiatricky, Prague, Czechoslovakia /A differential approach to the indication of neuroleptics./ Diferencialni indikace neuroleptik. ***Activitas Nervosa Superior (Praha).*** **12(1):1-11, 1970.**

The therapeutic values of some neuroleptics were compared under the conditions of a controlled multiclinic experiment. Prochlorperazine, perphenazine, trifluprомazine and chlorpromazine possessed significant therapeutic effects in the therapy of paranoia with Phenobarbital and mepazin were effective in cases with hallucination and disorientation, emotional reactivity and conceptual disorientation. Interesting results were obtained in depressive states and anxiety. The most effective drug was trifluprомazine; perphenazine was less effective. Prochlorperazine and chlorpromazine showed approximately the same effects. The lowest therapeutic value was found with phenobarbital and mepazin. The results obtained in anxious - phobic and neurotic patients revealed a remarkable improvement after imipramine and significant worsening of symptoms after chlorpromazine. 15 references.

070925 Vojtechovsky, M. Vladislava Vancury 15, Prague 5, Czechoslovakia /New findings in the clinical pharmacology of sleep./ Nektere novejsi poznatky o klinicke psychofarmakologii spanku. ***Activitas Nervosa Superior (Praha).*** **12(1):12-21, 1970.**

A review of new findings in the clinical pharmacology and neurochemistry of sleep was presented including the pathology of sleep in patients with mental and emotional disorders and a survey of pharmacologic agents influencing the syndrome of sleep deprivation. The psychopharmacology of sleep represents a new discipline which, in its present state, is only an accumulation of facts. 77 references.

070970 Klein, Donald R. Hillside Hospital, Glen Oaks, New York Psychotropic drugs and the regulation of behavioral activation in psychiatric illness. ***In: Smith, W., Drugs and cerebral function.*** **Springfield, Illinois, Charles C Thomas, 1970. 288 p. (p. 69-81).**

The theory that central dispositional states can exert facilitatory or inhibitory influences over behavior is discussed. Early models using the terminology of 'habit' and 'drive' are considered. The effect on behavior of energizers such as amphetamines and depressants such as phenothiazines are related. Models are proposed to explain the mechanisms by which such psychoactive drugs have their effects. One model, the rheostat model, visualizes the drugs as nonselective regulators of psychic impulses. Certain inconsistencies of this model, such as the double effect of noradrenaline excess or deficiency on mania or depression, are pointed out. Patients suffering from schizoaffective disease, for example, are normalized by phenothiazine treatment whether depressed or excited. The 'thermostat model' has arisen as an alternative to the 'rheostat model'. It states that psychotropic drugs act selectively to affect pathological disturbances in a normalizing manner and do not act in a compensatory fashion (as aspirin acts to lower body temperature only in the hyperthermic state). The strengths and weaknesses of this theory are discussed. 32 references.

070971 Conners, C. Keith. Child Development Laboratory, Massachusetts General Hospital, Boston, Massachusetts The use of stimulant drugs in enhancing performance and learning. ***In: Smith, W., Drugs and cerebral function.*** **Springfield, Illinois, Charles C Thomas, 1970. 288 p. (p. 85-98).**

The psychological effects on children with cognitive and behavioraldeficits of amphetamines, methylphenidate and deanol, all CNS stimulants, are reviewed. Behavioral disorders in children, characterized by disruptiveness, aggressiveness and lack of interest in schoolwork, show marked improvement with benzedrine or dextroamphetamine treatment as shown in several separate studies. Simple cognitive functioning, such as arithmetic performance, is enhanced by stimulant drugs, although there is a question as to whether this is real improvement, or simply an offsetting of fatigue or other deficit states. Tests requiring vigilance and alertness show improvement and the Porteus Maze Performance test has shown marked improvement in children treated with Ritalin and Dexedrine. Results of several clinical and controlled studies on deanol give conflicting indications as to its efficacy, although the controlled studies used smaller doses to avoid any side-effects. 55 references.

070975 Werry, John S. Institute for Juvenile Research, Chicago, Illinois Some clinical and

laboratory studies of psychotropic drugs in children: an overview. *In: Smith, W., Drugs and cerebral function.* Springfield, Illinois, Charles C Thomas, 1970. 288 p. (p. 134-144).

The effects of phenothiazines and stimulants on clinical and laboratory behavioral parameters of children are reviewed on the basis of several studies. Stimulants, such as dextroamphetamine and methylphenidate, improved attention at home, reduced inappropriate behavior (e.g. hyperactivity) and increased teacher pupil interaction at school. In the laboratory, task performance was generally improved in regard to tasks involving vigilance, speed of response, short-term memory and simple motor skills. For phenothiazine stimulants, there is good correlation between clinical and laboratory measures withimprovement of behavior apparent in both situations. The phenothiazines reduced inappropriate motor behavior (hyperactivity) and slightly reduced positive teacher pupil interaction. They affected task performance adversely under certain conditions, and were found to have no consistent effect on motor activity. Clinical and laboratory correlation was not found to be good for phenothiazines and this class of drugs was found to be weakly depressant on arousal levels. Special difficulties attending drug trials in children are discussed. 17 references.

070976 Essman, Walter B. Psychology Department, Queens College of the City University of New York, Flushing, New York Central nervous system metabolism, drug action and higher functions. *In: Smith, W., Drugs and cerebral function.* Springfield, Illinois, Charles C Thomas, 1970. 288 p. (p. 151-175).

A discussion is presented proposing a model system to correlate central nervous system changes resulting from drug action with behavioral function. The effect of electroconvulsive shock (ECS) in decreasing brain RNA levels are described, and a relationship with amnesic events following ECS is proposed. The effects of lithium carbonate treatment in animals on brain magnesium and serotonin levels are described and discussed in relation to manic-depressive illness. The effects of imipramine in causing high amplitude slow (EEG) waves and in suppressing arousal in animals are discussed, although this drug is not known to modify significantly behavior in animals. RNA alterations (increase in neurons, decrease in glia) and enhanced cytochrome oxidase activity are discussed. Considerations such as dosage, brain uptake and the nature of electrolyte and metabolic changes should be investigated in attempting to unify preventive chemotherapy and brain function. 68 references.

070982 Johnson, Merlin H. 4435 Beacon Avenue South, Seattle, Washington 98108 Drugs in the management of depression. *Northwest Medicine.* 69(10):780-784, 1970.

The efficacy of various drugs in the treatment of depression is considered. In choosing drugs for the management of depression, it is important to determine the severity of the depression. (Nonpathological situational depression is not amenable to chems therapy). Three types of depression are distinguished: anxious depressions; hostile depressions; and retarded depressions. Stimulants have no general usefulness in treating depression, sufficient quantity causing increased agititation and discomfort, increased danger of attempts at suicide, and habituation. Sedatives, such as barbiturates, and antianxiety drugs, such as the glycerol derivatives, the diphenylmethane derivatives, and the benzodiazepine derivatives, do not usually improve the patients' mood. Sedatives may reduce agitation or tension, but because of the possibilities of drug dependence, they are unsatisfactory except for short term use. Habituation is a hazard with the antianxiety drugs after heavy use. The tricyclic antidepressants have anticholinergic side-effects, and potentiate other drugs; the onset of therapeutic action is slow. Antipsychotic agents may control agitation without improving the depressed mood, and are sometimes used with the antidepressants. Typical treatment for a depressed patient is 25mg twice daily of imipramine or amitriptyline, adding 25mg every second day up to 150mg daily. ll references.

071027 Brill, Norman Q.; Crumpton, Evelyn; Frank, Ira M.; Hochman, Joel S.; Lomax, Peter; McGlothlin, William H.; West, Louis Jolyon. Department of Psychiatry, University of California at Los Angeles School of Medicine, Los Angeles, California The marijuana problem. *Annals of Internal Medicine.* 73(3):449-465, 1970.

In an interdepartmental conference on the marijuana problem at the University of Southern California, contributions were made on the pharmacology of marijuana, clinical studies of its effects on man, prevalence of its use in colleges

and high schools, personality characteristics of users, effects of long-term use, and the implications of marijuana use for the society at large. Marijuana, derived from the plant Cannabis sativa, is unusually safe compared to alcohol or barbiturates. It causes no physical dependence or tolerance, but psychic dependence and habituation do occur. The intoxicating properties of the plant are found in the derivatives of cannabinol, in particular 2 isomers of tetrahydrocannabinol, which can now be synthesized. Animal studies with tetrahydrocannabinol show a reduction in individual and group aggression, and temporary disruption of social hierarchies. The median lethal dose of tetrahydrocannabinol in mice is about 1500mg/kg, and in dogs, 10g/kg body weight. Clinical studies on man, using an average of 2g marijuana containing 1 percent tetrahydrocannabinol, indicated little if any impairment on simple psychological and perceptual motor tests. The prevalence of marijuana use in colleges averages 24 percent for those who have already tried marijuana, and in high schools the average is 22 percent. In studies of personality differences between users and nonusers, greater use of marijuana was related to higher scores on the stimulus seeking scales and the psychopathic deviate scale. More males than females report using the drug daily. Some clinics believe that personality changes occur in chronic users, and some see drug abuse as a symptom of dissatisfaction with the present values and direction of society. 29 references.

071314 Gearing, Frances Rowe. Division of Epidemiology, Columbia University School of Public Health and Administrative Medicine, New York, N. Y. Successes and failures in methadone maintenance treatment of heroin addiction in New York City. (Unpublished paper). New York, Methadone Evaluation Unit, 1970. 12 p.

Successes and failures in methadone maintenance treatment of heroin addiction by the Methadone Maintenance Evaluation Unit in New York City are reported for the period 1965-1970 and recommendations for further services are made. On balance, the successes in the Methadone Maintenance Treatment Program far outweigh the failures. The rapid expansion of the program during 1969-1970 and the change in emphasis to include primarily ambulatory induction under the expanded admission criteria does not appear to have made any noticeable change in the effectiveness of this treatment for those heroin addicts who have been accepted into the program. A majority of the patients have completed their schooling or increased their skills and have become self-supporting. Their pattern of arrests has decreased substantially. This is in sharp contrast to their own previous experience, as well as their current experience when compared with a matched group from the Detoxification Unit, or when compared with those patients who have left the program. Less than 1% of the patients who have remained in the program have reverted to regular heroin use. A small proportion of the patients (10%) present continued evidence of drug abuse involving use of amphetamines, barbiturates and cocaine, and another 8%demonstrate continued problems from chronic alcohol abuse. These 2 problems account for the majority of failures in rehabilitation after the first 6 months. It is concluded that any treatment program using methadone maintenance must be prepared to provide a broad variety of supportive services to deal with problems including mixed drug abuse, chronic alcoholism, psychiatric or behavioral problems and a variety of social and medical problems. (Author abstract modified)

072219 Serry, David; Serry, Maurice. Royal Park Psychiatric Hospital, Parkville, Victoria, Australia Masked depression and the use of antidepressants in general practice. *Medical Journal of Australia (Sydney).* 1(7):334-338, 1970.

Depressive states are common in general practice but masked depressive states are often missed in a diagnosis due to a paucity of significant symptoms. There may thus be a place for the use of an adequate therapeutic trial of antidepressants, once organic lesions have been excluded. Further investigation of the incidence of depressive states in general practice is called for with this group being studied separately from other neuroses. 4 references. (author abstract modified)